Exhibit 22

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE: ACETAMINOPHEN – ASD-ADHD PRODUCTS LIABILITY LITIGATION	)	MDL No. 3043
	)	Case No. 1:22-md-03043-DLC
THIS DOCUMENT RELATES TO: All Cases, 1:22-md-03043	)	JUDGE DENISE COTE

WEDNESDAY, AUGUST 2, 2023

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

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Videotaped deposition of Robert Cabrera, Ph.D., held at the offices of Tracey Fox & Walters, 440 Louisiana Street, Suite 1901, Houston, Texas, commencing at 8:55 a.m. Central, on the above date, before Carrie A. Campbell, Registered Diplomate Reporter, Certified Realtime Reporter, Illinois, California & Texas Certified Shorthand Reporter, Missouri, Kansas, Louisiana & New Jersey Certified Court Reporter.

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EXHIBITS

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VIDEOGRAPHER: We are now on the record. My name is Brian Bobbitt. I'm a videographer for Golkow Litigation Services.

Today's date is August 2, 2023, and the time is 8:55 a.m. Central Time.

This video deposition is being held in Houston, Texas, in the matter of Acetaminophen, Tylenol, ASD/ADHD Products Liability Litigation for the United States District Court, Southern District of New York.

The deponent is Robert Cabrera.

Counsel will be noted on the stenographic record.

Our court reporter may now swear in the witness.

ROBERT CABRERA, Ph.D., of lawful age, having been first duly sworn to tell the truth, the whole truth and nothing but the truth, deposes and says on behalf of the Defendant Johnson & Johnson, as follows:

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DIRECT EXAMINATION

QUESTIONS BY MR. MURDICA:

Q. Good morning.

A. Good morning.

Q. Could you state your name for the record.

MR. TRACEY: Jim? Jim, can you hear me?

MR. MURDICA: Yes, sir.

MR. TRACEY: Yeah. So before we get started, I think Rebecca has four or five articles that when Robert was preparing, he looked at his notes and found them, and they were not on his MCL. She's going to give those to you.

There's also one article that was published like from two days ago, and until we get our agreement on how to supplement the articles that are continuing to come out, we thought we better hand it to you this morning.

So Rebecca is going to give that to you now before we start, those -- those articles.

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MS. KING: Okay. And I counted seven.

MR. TRACEY: Okay. Sorry.

MR. MURDICA: All right. Let's try this again. Anything else before we get started?

MR. TRACEY: No, no, no. Sorry about that.

MR. WATTS: Welcome to Houston, Jim.

MR. MURDICA: Yeah. Yes, I'm sure those couldn't have been transmitted earlier than right now. Thank you.

QUESTIONS BY MR. MURDICA:

Q. Good morning.

A. Good morning.

Q. Please state your name for the record.

A. Robert Matthew Cabrera.

Q. Robert Matthew Cabrera, we've never met before right now; is that correct?

A. That's correct.

Q. How do you refer to yourself?

A. Robert.

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Q. Okay. How would you like me to refer to you during this deposition?
A. Okay.
Q. Dr. Cabrera, what are your qualifications as a doctor, sir?
A. I have a doctorate in medical sciences.
Q. Are you a medical doctor?
A. I'm a medical scientist, not a medical doctor.
Q. Are -- I understand you're part of a lab.
Do the other people in the lab refer to each other as doctors when they're not medical doctors?
A. If you're in the lab, we refer to each other as first names. If you're outside of the lab, then we generally refer to each other by our titles.
Q. Okay. And you understand you're here in relation to a litigation, correct?
A. Yes, I do.
Q. And that's not your normal work; it's not litigation, right?

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A. No. It's not my normal, everyday job.
Q. Okay. Who employs you in your everyday job?
A. Baylor College of Medicine.
Q. Does Baylor College of Medicine know that you're here today?
A. I'm on vacation.
Q. Okay. Does Baylor College of Medicine know the opinions that you've put forth in this litigation with respect to the acetaminophen?
A. I'm not submitting them on behalf of Baylor.
Q. Okay. So they have not taken a position one way or another whether it's appropriate for you to opine on acetaminophen outside of work?
A. I have not.
Q. Okay. Do they know you're doing this work?
A. They do not.
Q. Your training is primarily in teratology; is that right?
A. That's correct.

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Q. Okay. And your focus through your career thus far has primarily been neural tube defects and major congenital malformations, right?
A. I work primarily in neural development, which includes neural tube defects.
Q. Okay. Has your focus in neural development been neural tube defects?
A. Predominantly, yes.
Q. And predominantly it's been in identifying causes and finding protective measures to prevent them; is that fair?
A. We look at both the cause and the prevention of birth defects, including neural tube defects.
Q. And in this litigation, you submitted an expert report in June; is that right?
A. That's correct.
Q. It was about 200 pages?
A. Approximately.
Q. A week later you amended your report, correct?
A. That's correct.

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Q. Okay. Why did you amend your report?
A. There was some minor edits that needed to be corrected that we had noticed.
Q. What do you mean "we had noticed"?
A. Well, reading through the documents afterwards, it was -- there were some things that were done that were left incomplete and needed to be corrected.
Q. So were they things you added to or things you corrected?
A. Corrections, just corrections that were made.
Q. Did you remove anything?
A. Specifically, I don't -- I don't recall that we removed anything.
Q. You don't recall that you removed anything?
A. No.
Q. Did you add anything?
A. Edits. There was edits as far as -- just edits.
Q. Typos or anything substantive to your recollection?

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A. Not anything substantive, just typos, typographical errors.
Q. So between your original report and your amended report a week later, there were no substantive changes?
A. I didn't make any substantive changes, no.
Q. Okay. At some point you provided a further supplemental report related to one article, correct?
A. That's correct.
Q. And just now I was handed additional articles.
Are those articles that you've reviewed?
A. Yes, they are.
Q. Okay. Are they articles that you have additional opinions about?
A. They're consistent with my opinions that I've put forth in my report and my supplemental.
Q. Okay. Is there anything you reviewed since your supplemental report that's not consistent with your report that you haven't provided?

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A. No.
Q. Okay. Do you have a draft of an additional report in the works now or anything like that?
A. I think -- I haven't started a new draft, no, not for the --
Q. So as of today, I have in writing whatever your opinions are, correct?
A. I believe so, yes.
Q. Okay. I want to talk to you a little bit about teratology in early pregnancy in particular.
In the first 14 days of pregnancy, do you generally agree that any teratologic event is an all-or-nothing event?
A. Classically that was believed. That is not necessarily the case, and that's been shown with -- particularly with alcohol and retinoic acid. Those are exceptions.
Q. There's been so few mitoses in the first few days of pregnancy that an environmental effect or a teratological effect would most likely kill the embryo.
Is that fair?
A. Classically, that's -- that's

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the way it was presented. The hypothesis would put forth that there was an all-or-nothing effect.
What has been shown is that early exposures, even before organogenesis with specific teratogens, have been noted to be able to produce malformations and not necessarily produce an all-or-nothing with those early exposures, and two of those examples would be retinoic acid and alcohol.
Q. Okay. And going beyond the 14 days, there are some structural defects that can be induced by teratogens, right?
A. Yes.
Q. And with time, we've come to learn that some of them are induced at specific times, like cleft lip, for example.
Is that fair?
A. There is what's referred to as critical windows of exposure that tend to define when particular organ systems are susceptible to teratogenic effects of teratogens.
Q. And is one of those cleft lip?
A. Yes. There's a -- there's a

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time window as well for clefting or cleft lip.
Q. And would you say 21 to 28 days is the key window for that?
A. That would actually be a little bit early for cleft lip.
Q. Is that anything that you've ever studied, Doctor?
A. Cleft lip?
Q. Yes.
A. Yes.
Q. And specifically the teratologic window for cleft lip?
A. Yes.
Q. Okay. How about for autism? What's the teratologic window for autism?
A. So the neurodevelopment in the human, it's continuous with neurulation, which is the start of neural tube closure and continues throughout gestation through both the second and the third trimester of pregnancy.
Q. Yeah, okay. And I'm asking specifically about autism.
When is the teratologic

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effect that can -- I assume your testimony here is that a teratologic effect can cause autism in development, right?

A. Yes.

Q. And when is the window for that teratologic effect for autism specifically, not neurodevelopment?

A. Right. Well, it coincides because autism is a neurodevelopmental disorder. A teratogenic effect that occurs during its critical window of exposure, which includes development of the nervous system, and the development of the nervous system continues throughout gestation, both the second and third trimester.

Q. Okay. And so when would be the first window that a teratogen can affect the neuro -- neurological development?

A. So we've shown that -- in the animal model that it coincides with neurulation, so we can do exposures as early as eight and a half days of gestation which is the beginning of the neural tube closure, which would coincide with approximately, as you mentioned, 14 to 28 days in pregnancy.

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And during that critical window of exposure in the animal model, we're able to produce autism in animals that have been exposed during neurulation, so as early as neurulation, but continues throughout pregnancy.

Q. Okay. So is it fair that the most critical -- to say that the most critical window to induce autism in the opinion of Dr. Cabrera is 14 to 28 days of the human pregnancy?

A. That is not my opinion, no.

Q. Okay. Please state for the record Dr. Cabrera's opinion as to the most important time for a tera -- teratogenic inductions of autism in human pregnancy.

A. So --

MR. TRACEY: Objection. Form.

THE WITNESS: So throughout neurulation and neural development, that is the critical window of exposure. I think the time of most sensitivity would be during the second trimester of pregnancy.

And that's been supported by

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animal models and also consistent with the studies of fever in humans.

QUESTIONS BY MR. MURDICA:

Q. A neural tube defect, which you referred to earlier in the early part of neurologic development, that would be much more profound than autism, correct?

A. Yes. It's a severe congenital malformation. It's often not compatible with life.

Q. When you were first -- you're a member of the Teratologic Society, right?

A. I -- what was referred to as the Teratologic Society, which I still like to think of as the Teratologic Society, I am still a member, yes.

Q. You're still a member.

You're not a member -- are you familiar with OTIS?

A. I -- I am.

Q. You're not a member of that, are you?

A. I am not.

Q. Were you ever invited to be?

A. No, I haven't applied.

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Q. Okay. When did you first take an interest in autism in particular, Dr. Cabrera, in your research?

A. So for the last five years, I've been working on another compound that was associated with neural tube defects, and part of what we're doing is behavioral testing.

So that's when I started to look at interactions and some overlap between early neural development and autism spectrum disorder, behaviors in animal models.

Q. And you're doing that at Baylor?

A. Yes.

Q. And what's the compound?

A. Dolutegravir. It's an HIV antiviral.

Q. And is that funded by any particular company?

A. It's funded by the National Institutes of Health, the National Institutes of Mental Health.

Q. Whose drug is that, if anybody's, or is it an old drug?

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A. No. No. It's -- I can double-check on that, but maybe Gilead.
Q. Okay. I want to talk to you a little bit about the human brain for a minute.
Where in the human brain are the features that result in autism?
A. So different parts of the brain have been associated with autism. I don't know that there's any one portion of the brain that specifically causes autism as a neurobehavioral disorder.
Q. So, in other words, whatever -- well, do you believe that there are structural abnormalities in the brain of patients with autism?
A. Those have been documented in -- and, you know, one example is there was a publication in the New England Journal of Medicine by Stoner that demonstrated what I -- what I refer to as neural layering defects, and those are predominantly in the frontal and occipital cortex.
Q. But your testimony here today is that the structural manifestations of

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autism can be in any portion, any anatomic portion, of the human brain?
A. Well, not any anatomic portion. It would be predominantly those involved in executive function, reasoning, although some other ones have demonstrated that there's also some cerebellar involvement in some patients with autism.
Q. So what -- tell us the anatomic regions of the brain where there would be structural changes that are a part of autism or indicative of autism?
A. So what's been documented includes impacts on the neural laminal layers, which -- largely different areas of the cerebral cortex and then also the cerebellum.
Q. Okay. How about the hippocampus?
A. There is some data to support interaction with the hippocampus as well.
Q. Okay. And I -- you used the word "interaction." I didn't ask about interaction.
Are there structural changes in

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the hippocampus that are either signs or causal for autism?
A. There have been documented some structural changes. Actually, one of the papers we gave you today shows some structural changes in the hippocampus that were associated with acetaminophen exposures, particularly in the autism model.
Q. Yeah. And my questions were about human beings, and I think what you're referring to is a study in mice, correct?
A. That is correct.
Q. Out of Wuhan, China?
A. Yes.
Q. Are you familiar with the lab there?
A. I'm -- not particularly.
Q. How important is your reliance on a mouse hippocampus study from Wuhan, China?
A. It's part of the totality of evidence. I've considered it.
Q. Okay. But you had the opinions you're going to talk to us today before seeing that study, right?

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A. Yes.
Q. At what point did you come to the conclusion that acetaminophen -- acetaminophen causes autism -- well, we'll -- do -- we'll take it one at a time.
At what point in time did you come to that opinion?
A. So while I was reviewing the literature systematically, I realized that there was a -- had accumulated an overwhelming amount of evidence that supported that position.
Q. Okay. And was that in 2023?
A. Yes, that's this year.
Q. Okay. And were you doing that -- were you systematically reviewing the literature for fun or for some other reason?
A. Because I was asked to.
Q. Okay. You were asked to, not for your job, right?
A. For the -- for why I'm here today --
Q. Yeah.
A. -- as a consultant.

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Q. And I'm going to ask you the same question for ADHD.
At what point in time did you come to the conclusion that acetaminophen causes ADHD in human beings?
A. It's concurrently.
Q. In other words, concurrently in 2023?
A. Yes.
Q. Had you ever looked at literature on acetaminophen and autism prior to 2023?
A. I looked at literature on acetaminophen generally, and I had also been following it sometime during COVID, but not -- hadn't conducted a systematic review.
Q. Right.
And hadn't conducted a review with respect to autism or ADHD in particular, correct?
A. Incorrect. I had been reviewing studies, particularly the meta-analysis that had been published in the last several years for my own class.
Q. And what class is that? The

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nutrition class?
A. No. I also teach two other classes. One of them is medical biochemistry, in addition to a genetic counseling class, and it was for the genetic counseling class.
Q. Okay. And what degrees or board certifications do you have in genetics?
A. I'm not a -- my boss is a board-certified geneticist. I'm not a board-certified geneticist.
Q. And why are you talking about your boss?
A. Well, the class, I was referred to as being able to teach this class. And so that was who referred me as a -- said that I could teach the class.
Q. Does your boss teach the class, or do you teach the class?
A. I teach the class.
Q. Okay. So you teach a class about genetics and are not certified in genetics in any way, correct?
A. Well, the person -- again, my boss, and then also the person that is the

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primary instructor, is certified in genetics. So I'm a lecturer in that class.
Q. Oh, I see.
So the class, if we looked at a syllabus -- or the class is actually taught by your boss?
A. So, well, my boss's colleague.
Q. Correct?
Okay. Now I'm just confused.
If we went and looked at the program for the school, does it say Dr. Cabrera is the professor?
A. As a lecturer.
Q. Okay. So much like I go to Baylor as a guest lecturer in a law class, that doesn't make me a professor, correct?
A. No, not unless you're appointed a professor.
Q. Okay. Are you appointed a professor?
A. Associate professor.
Q. In -- at Baylor or at UT or where?
A. At Baylor.
Q. Okay. Where do you teach your

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nutrition class?
A. So I'm not currently teaching my nutrition class. I was teaching it at San Jacinto College and also UT in Austin.
Q. And your nutrition class, was that more in the vein of maternal nutrition to prevent neural tube defects?
A. It's, let's say, a core class. So we were required to teach a class as part of our faculty appointment, and I was teaching a core credit class in nutrition. So it was a general science class.
Q. Was that the first class you were -- you ever regularly taught?
A. No, it was not.
Q. Okay. What was the first class you ever taught?
A. I -- before that, I was teaching a class in the philosophy of science as well.
Q. And does the philosophy of science have anything to do with autism or ADHD?
A. It did not, no.
Q. Okay. And you said you teach a

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biochemistry class right now?
A. That's correct.
Q. And what degrees do you have in chemistry or biology or biochemistry?
A. I trained in biology. That's my -- my undergrad was in biology.
Q. Okay.
A. And the class that I teach, I teach genetics in that class. That's -- I cover the genetics lecture in that class. So I'm the lecturer in that class.
Q. And is the audience medical students?
A. There's two different audiences. One is graduate students. We have a graduate student section, and then I also teach a professional student section, which is physician's assistants and orthopedic and nurse anesthesiologists. So not medical students, professional students.
Q. Okay. I asked you a couple minutes ago about when you first became interested in autism, and I think you said you've been working on a compound for the last five years in relation to that.

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How does the compound that you're doing -- how does your research relate to autism? Is it whether the drug induces autism?
A. So initially there was a report that there was neural tube defects in Botswana that happened just over five years ago, approximately five years, and we followed up that study with producing an animal model of that that would show that it was fully responsive. And we've followed that up with now a mouse model that's also shown that it's fully responsive just to show that this drug can produce neural tube defects that are fully responsive.
Q. Okay. And I asked you about autism.
A. Right.
Q. Autism is not neural tube defects, correct?
A. And then the -- on the follow-up for that, we were also funded to look at the neurological impacts because these are also associated with neurological problems in people -- both adults taking the

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medication and so we looked at that as well.
And so while we were doing behavioral studies on those animals, we also looked at the effect of in utero exposure on the behavior of offspring, and that was where we started to look at autism.
Q. Okay. And that was a -- you said that was a follow-up grant, right?
A. That was -- yeah, that was a follow-up.
Q. When did you get that follow-up grant?
A. About three years ago.
Q. Okay. So is it really three years then you've been looking at autism?
A. Well, that's when we got the grant to look at that, yes.
Q. And then you began after that, correct?
A. Right. Right.
Q. Okay. So it's not five years. You weren't studying autism five years ago, correct?
A. Initially we were studying neurodevelopment, and then that led into us

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studying autism.
Q. Okay. And it wasn't specifically autism that you were studying. Even in the last three years, it was neurological effects of that compound, correct?
A. That is correct.
Q. That includes more than autism, right?
A. Yes.
Q. What else does it include?
A. Well, in human patients, it's predominantly what's referred to as adverse events. And so adverse events reported included things like headache in patients, potentially, and other, I guess, complaints that were neurological in people that were taking the medication.
Q. And has this research been published?
A. The neural tube defects paper was just published, I believe, a couple weeks ago.
Q. Uh-huh.
A. And the behavioral studies we

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haven't published yet.
Q. Are you intending to?
A. Yes, we do.
Q. Okay. What, if any, conclusions did you come to as to what you're calling behavioral effects of that compound?
A. So we've seen increased activity in those animals that we documented in open field testing.
Q. And what does that increased activity mean to you?
A. Well, there's different interpretations, but potentially anxiety in the animals.
Q. Okay. And does the anxiety allow you to opine that that compound causes any particular neurologic effect or defect?
A. Yeah. So we follow that up with looking at the brain and doing brain pathology, and also metabolomics on the brain as well.
Q. Okay. So you sacrifice the animal and examine the mouse brain?
A. Yes.
Q. Okay. And what conclusions, if

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any, did you draw between that compound and causation as to any particular neurologic effect?
A. Suffice it to say, we do see changes in single carb metabolism that appears to be affecting dopaminergic pathways, but we haven't drawn any conclusions other than the fact that there -- the animal has increased anxiety at this point.
Q. Okay. So increased anxiety in a mouse model doesn't necessarily mean that it causes any particular neurologic defect?
A. It can be consistent with other problems, but we haven't seen other problems in the animal. That was one of the things that we noted that was statistically significant in the study that we did.
Q. And what other problems would you look for?
A. So some of the things that can be looked for is we also do three-chamber for socialization. We didn't see changes in socialization in that animal.
Q. Okay. And if you had, then it

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might change your conclusion? Is that what you're saying?
A. Yes.
Q. Okay. So if we went and looked at the grant that you got that you're talking about for this compound, would it say that you were investigating autism?
A. It does not.
Q. Okay. Would it say that you're investigating ADHD?
A. It would not.
Q. Okay. So is this work that you're doing here, this is the first time you actually examined specifically autism and ADHD in relation to any particular environmental exposure.
Is that fair?
A. That is not correct.
Q. Okay. What else have you -- what other work have you done evaluating autism and ADHD as an outcome to an exposure?
A. When I was in graduate school, we also did a behavioral study looking at the exposure of valproic acid and heavy metals in autism core behaviors.

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Q. Okay. And that -- was that in a particular lab in grad school?
A. Yes, it was.
Q. And is it the same lab you work in now?
A. Well, we've come a long ways, but, yes, I still work for the same person.
Q. Okay. So in grad school, was that Richard Finnell's lab?
A. Yeah, he was the director of the institute and also the PI of the lab.
Q. And he was looking at Depakote, or valproic acid, and neurologic outcomes?
A. Not exactly. A colleague of mine, Denise Hill, was interested in heavy metal toxicity, and we appreciated that valproic acid was the model for autism in animal models, particularly in mice. And so we compared heavy metal exposure with valproic acid in those animal models.
Q. To what endpoint? To see if the heavy metal exposure could induce autism?
A. Autism-like behaviors, yes.
Q. Okay. And was that published?
A. Yes, it was.

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Q. Okay. And had you ever done neural tube defect research on valproic acid before that?
A. Yes.
Q. Was that also in your grad school research?
A. Yes, it was.
Q. Okay. So your role, when you were in grad school, I take it, you weren't a lead investigator or anything like that on that study?
A. In graduate school, I was -- well, one of those studies I was first author but not the PI of the study.
Q. Okay. How about the autism and valproic acid study, were you first author there?
A. I was -- Denise was the -- that was her first author publication. I followed, second author.
Q. And on that publication, if we looked at it, was that in an animal model, or were you making determinations as to human effects?
A. That was in an animal model.

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Q. Okay. So let me try again then.
Is this the first time you've ever opined that a compound -- an exposure can cause -- can induce autism in a human being?
A. Yes, it is.
Q. Okay. And you've never done that or made that conclusion outside of litigation ever before today in this year, correct?
A. Yeah, this is my first time offering an opinion on autism.
Q. Okay.
A. Or ADHD.
Q. Back to valproic acid.
Valproic acid has been known to be a human teratogen for decades, correct?
A. That is correct.
Q. It was one of the early antiepileptic drugs, the first -- first-line antiepileptic drug a long time ago, correct?
A. Discovered by chance, it was shown to be an effective antiepileptic drug.
Q. And those first-line

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treatments, like valproic acid and phenobarbital, those are known teratogens, correct?
A. Particularly valproic acid is -- they're potent teratogens.
Q. By the time you were in grad school, everybody agreed and knew that first-line AEDs could induce major congenital malformations in human beings, correct?
A. I would like to think that everyone knew, but there were still people defending the position that they didn't. I still argue incorrectly, but it was generally understood that they were -- caused birth defects.
Q. Well -- and that's one of the reasons that you used it in the mouse model, correct?
A. That's correct.
Q. All right. And one of the reasons that you knew that is because there had been prospective, double-blind pregnancy registries that showed a profound effect of valproic acid on human pregnancy, correct?
A. Well, there had been initially

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retrospective studies that had identified there was an effect of valproic acid, and then those were followed up by both animal models that demonstrated that, in addition to prospective studies in women with epilepsy treated and untreated.
Q. Okay. Are you familiar with the North American Antiepileptic Drug Registry?
A. I am.
Q. Do you know Lew Holmes?
A. I do.
Q. Sonia Hernandez-Diaz?
A. I've met her a couple of times.
Q. Okay. So you know -- you know how they conducted that registry, right?
A. Not at its inception, but I'm familiar with the work.
Q. You're familiar that it's a human exposure registry?
A. Ongoing.
Q. Ongoing.
In human pregnancies, right?
A. That's correct.
Q. With exposure to anti- --

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unknown, blinded antiepileptic drugs, correct?
A. A variety of them now, yes.
Q. And it's prospective. They're followed -- they're enrolled right at the beginning of pregnancy, right?
A. That's correct.
Q. Okay. And the Holmes and Hernandez-Diaz are blind to the patient and the drugs, right?
A. That is my understanding until the analysis is done.
Q. And it's double-blind, right?
A. I -- I'm not sure about the double-blinding. I'd have to check that particular publication you're referring to.
Q. Okay. Well, there's many publications, right?
A. Yes.
Q. The pregnancy registry, they constantly publish any time something becomes significant, right?
A. They publish updates regularly.
Q. Right.
And that level of evidence

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is -- would you agree it's about as good as you get in human pregnancy?
A. The combination of having an animal model, having first observed this prospectively -- or excuse me, retrospectively and then doing the prospective study, that's -- that is strong evidence.
Q. Okay. Well, I didn't ask you about the animal model.
A. Yeah.
Q. What matters to people now, we have double-blind, prospective pregnancy registry human evidence now today, correct?
A. That is -- we do.
Q. And if you ask anybody in the field what the best evidence is, they're not going to start talking about animal studies. They're going to talk about the North American Antiepileptic Drug Pregnancy Registry and the publications that came out of that, correct?
A. I disagree.
Q. Okay. You disagree because you think now that we have human evidence, the

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animal evidence is what matters?
A. Well, I disagree because I talk to physicians regularly that counsel women that take anticonvulsant drugs, and they quite often ask me what I see in the animal models to help inform them on the relative risk of medications that they use that don't have enough data on them.
Q. Are you talking about the third-line antiepileptics?
A. Well, looking at particularly the newer ones, yes.
Q. Well, you know -- you know there isn't registry data on those yet, right, because they haven't reached significance?
A. Well, yes, because there's not enough exposures in the database yet.
Q. Right. Right.
So I don't think we're understanding each other because I'm asking you about drugs when we have human data, and we do have a publication because it did become significant in the registry.
Okay?

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For those drugs, not the newer ones, for those drugs, nobody is talking about the animal data. They're talking about the actual human data that became significant in a prospective, double-blind pregnancy registry, correct?
A. That's largely what you will hear about as far as -- for clinical analysis.
Q. That's the highest level of evidence you can get in human pregnancy within the bounds of current ethics, correct?
A. Well, in addition to that, that can be distilled further into meta-analysis. That would be the best set of data.
Q. If there's multiple studies.
A. If there's multiple studies.
Q. Okay. All right. And valproic acid has had a major congenital malformation warning on the label, as the drug Depakote, for decades, correct?
A. As far as I know, yes.
Q. Okay. And then eventually, after it was already, essentially, not used in pregnancy unless no other AED would work,

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an autism warning was added to it, correct?
A. That is correct.
Q. Okay. Throughout your reports you mentioned many times an adverse outcome pathway.
A. (Witness nods head.)
Q. In particular, an AOP 20. Do you remember including that in all of your reports --
A. Yes, I do.
Q. -- or at least your original report, your amended report and your supplemental -- your rebuttal report all have AOP 20, correct?
A. That is correct.
Q. Okay. And what organization came up with that pathway?
A. Well, that was published by the OECD, is -- it's where I found that originally.
Q. Okay. And what is the basis behind OECD? How do you know about them, and how do you use them in your regular work?
A. So the AOPs themselves I'm familiar with because I've done some work

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with the EPA in the past, and it's common for us to put AOPs together; to look for the existing evidence on a particular molecular interaction and whether it can have an impact on an organism; and how it has an impact on the organisms and whether there's any gaps in the data on having that impact on an organism.
Q. Okay. And the AOP 20 that you refer to a lot, you didn't publish that or put that together, correct?
A. I did not. That was independently done by researchers I -- I'm unfamiliar with before I had seen the AOP.
Q. Okay. And did you see that AOP for the first time in connection with this litigation?
A. Yes. It was published, I think, while I was doing the review of the literature for this litigation.
Q. Okay. And you mentioned EPA. You mean the Environmental Protective Association?
A. Agency, yes.
Q. Agency. Agency.

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You don't know if FDA uses AOPs, do you?
A. I'm not familiar with them using AOPs.
Q. You've never seen them using an AOP, correct?
A. Like I said, I'm not familiar with their use --
Q. By --
A. -- by the FDA.
Q. By the way, have you ever been contacted by the FDA for assistance with regard to any particular compound?
A. Yes, I have.
Q. Okay. And is it the one that you were -- that you were talking about earlier that you're working on now?
A. Well, with the entire class of molecules, the HIV integrase inhibitors, I was asked to go with the -- with the FDA, with the World Health Organization at the National Institutes of Health and National Institutes of Child Health and Development and present the work I had done on that compound.

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Q. Okay. And that was a -- some sort of meeting?
A. It was a meeting, yes, a conference.
Q. And when was that?
A. I believe it's approximately six years ago now. I think I have it on my résumé for a conference I attended.
Q. Okay. So that was the neural tube defect work that was funded by the National Institutes of Health?
A. It ultimately led to the funding of that work, yes.
Q. Led to the funding of the work. And then at some point you presented at a conference, and were you presenting on behalf of FDA?
A. No. I was meeting with -- it was a conference with shareholders in the medications, different shareholders for each one of the HIV antiviral integrase inhibitors, and we met with them in addition to the FDA and the World Health Organization.
Q. Okay. So who asked you to attend that meeting?

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A. The NIH.
Q. Okay. So not the FDA?
A. Well, the NIH would -- who had contacted us. The FDA was there also.
Q. Right. I understand they were there.
My original question was whether the FDA ever asked you to do any work in particular on a compound.
A. Right.
Q. And FDA has not asked you to do work on a compound, correct?
A. Well, multiple organizations that were -- that were asking for that.
Q. Let me try this again. FDA didn't invite you to that conference, correct?
A. It's hosted by the NIH.
Q. Okay. Did you have any contact with the FDA other than talking to them at that meeting?
A. Yes, I did.
Q. Okay. What was that?
A. Other people at the -- at the FDA had contacted me, and I had some

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correspondence with them about the work we were doing.
Q. Okay. Before or after the meeting?
A. Both.
Q. Okay. And it was in regards to those compounds --
A. Yes.
Q. -- correct?
Did they ever -- ever ask you for -- to provide them a report or any specific research?
A. They did ask for the data that we were -- that we planned on presenting.
Q. And this was all with regard to neural tube defects, correct?
A. Yes, it was.
Q. Okay. Back to the -- to the AOP.
Is AOP 20 the only AOP that is important to your opinions here?
A. Well, in addition, there was also another publication that came out in regards to the cannabinoid pathway, which was also another adverse outcome pathway that was

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published by -- not an OECD publication but an independently published.
Q. Okay. And the reason I'm asking about AOP 20, you mentioned your heavy metal research just a little bit ago.
AOP 20 is about using mercury to induce neurologic effects, correct?
A. The primary compound that is described in that AOP is mercury, but it also includes acetaminophen as a common compound that can also produce the same oxidative damage in -- in cells and produce the same outcomes.
Q. Well, the pathway itself has multiple steps, correct?
A. That's correct.
Q. And the one that's published that you're relying on uses mercury to induce the depletion of glutathione, right?
A. Well, they specifically look at mercury and the depletion of glutathione, in addition to the AOP cascade. And the analysis they conduct is then a weight of the evidence analysis on that AOP, specific to mercury.

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But they include acetaminophen as another compound that can produce the same effects as far as the oxidative damage and the interaction with thiol groups and specifically with glutathione.
Q. They do not, Dr. Cabrera, include acetaminophen as something that can be the first step to deplete the glutathione in that AOP, correct?
A. It's not in the group of compounds like mercury. It's not -- it's not listed with mercury.
Q. Right.
So the only place that -- if we look at it, and we probably will later today, the only place we would see acetaminophen is in a list -- in that pathway on the third step, I believe. It's in a list of stressors that once the glutathione is gone because of the mercury can induce damage in the pathway, correct?
A. That's not correct. It's a list of stressors that can produce the same biological effect, molecular and biological effect.

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Q. Okay.
A. And that is oxidative stress.
Q. Do you agree that step one only includes mercury and that step one is to deplete the glutathione so that there's no glutathione in the system, correct?
A. Well, there are other compounds listed in addition to mercury that can produce those effects.
Q. Okay. And the other compounds are other heavy metals that are not acetaminophen, correct?
A. They're not just heavy metals.
Q. Okay. They're not acetaminophen in the other compounds that can deplete the glutathione, correct?
A. Well, acetaminophen can deplete glutathione, but it's not specifically listed in the AOP with mercury. It's listed as a stressor in that pathway.
Q. Let me -- let me -- let me clarify that question because I think -- I think we're on the same page.
In the AOP 20, which you rely on in your report, acetaminophen is not part

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of step one of depleting the glutathione. That is not listed as one of the things it can, correct?
A. So, in the AOP, it's not listed with mercury in those first set of compounds.
Q. And then the next step or further down the cascade -- you used the term cascade, right? It's the pathway?
A. Yes.
Q. There's -- once the glutathione is depleted, there's the stressors, and there's a list of them, correct?
A. Generally speaking, the effect of glutathione can be made worse or can be caused by the stressors as well.
Q. And does it say that in the AOP?
A. It describes the effect of the stressors as creating oxidative damage, which is consistent with the same effect that the mercury and other compounds cause.
Q. But it doesn't say it in the AOP, correct?
A. It says exactly what I said.
Q. Okay. Did you look at the

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underlying -- you saw there were references for the list of stressors, correct?
A. Yes.
Q. Did you look at the underlying papers?
A. Yes, I did.
Q. Okay. And did you see the data for why acetaminophen is in there?
A. Why -- I'm familiar with the data, yes.
Q. Well, in the published -- in the literature references, there's nothing behind it, right? It's just acetaminophen is in a list of things that can cause -- potentially cause damage in the setting of depleted glutathione?
A. Well, acetaminophen itself can cause decreases in glutathione.
Q. I know you believe that, but that's not in the AOP, correct?
A. That's not a belief. That's supported by factual, scientific data.
Q. Well, it's -- Dr. Cabrera, it's not in AOP 20, is it?
A. It does deplete glutathione in

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AOP 20. It can cause depletion of glutathione.
Q. Okay. Okay. We're going to have to look at that because that's...
So your testimony right now is that AOP 20 says that acetaminophen depletes glutathione?
A. Not absolutely, but it -- certainly as a stressor, it can decrease glutathione.
Q. And you're saying that AOP 20 says that?
A. That as a stressor acetaminophen can decrease glutathione.
Q. Okay. Did you look into the other stressors that are listed in AOP 20 --
A. Yes, I did.
Q. -- do you recall them?
Okay. So furan, you saw that?
A. Furan, yes.
Q. Did you look at the literature behind that?
A. I'm familiar with it.
Q. Did you look at the references that are actually in AOP 20?

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A. Some of them.
Q. Okay. Do you know why not every -- not all the stressors that were listed in the reference literature were included in AOP 20?
A. Well, because they only did a weight of the evidence analysis on mercury.
Q. How do you know that?
A. It's evident in the document.
Q. So carbon tetrachloride isn't a stressor in the setting of mercury.
Is that your testimony?
A. It's -- it's listed in the AOP, but the AOP is specific in regards to a weight of an evidence analysis for mercury.
Q. Carbon tetrachloride is listed in the AOP?
A. We should -- we should look at the AOP for specific compounds. I don't remember them all.
Q. Okay. And the outcome -- because it's an adverse outcome pathway, the outcome is what in AOP 20?
A. Again, we should look at the document if you want a specific -- the

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specific language, but in regards to learning and development.
Q. Right.
In learning and development, you're using that as a marker for autism in your report, correct?
A. It's described in the document itself, that it can overlap with autism.
Q. Okay. Your testimony is AOP 20 describes in the document that learning -- decreased learning can overlap with autism?
A. That's correct. I quoted that -- those specific statements in my report.
Q. And you are relying on AOP 20 as proof that a pathway exists between -- well, it only has mercury in there, but a, I guess, demonstrative that such a pathway could exist between an exposure and autism, correct?
A. It doesn't only have mercury in there. It has other compounds, and one of those stressors includes acetaminophen interacting with the same pathway.
And as I'm well aware, it can

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also affect glutathione as part of its metabolism, just like mercury.
(Cabrera Exhibit 1 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Why don't we mark that, the AOP 20.
Okay. Is that the AOP that you have in front of you, Doctor?
A. Yes, it is.
MR. WATTS: Jim, what is the exhibit number?
MR. MURDICA: It is AOP 20 that's cited in this --
MS. KING: It's 1.
MR. MURDICA: Exhibit 1, yeah.
MR. WATTS: There you go.
MR. MURDICA: We didn't mark anything yet.
QUESTIONS BY MR. MURDICA:
Q. And, Dr. Cabrera, prior to this being -- well, is this -- is this published in peer-reviewed literature?
A. Yes, I believe it is.
Q. Okay. And where is it?

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A. I -- I'd have to look.
Q. Okay. You found this online, though, right?
A. It is correct.
Q. Not in any particular literature citation or anything like that?
A. Initially I found it online --
Q. Okay.
A. -- when I was searching the database for adverse outcome pathways.
Q. Okay. And have you ever been a part of the review for this adverse outcome pathway?
A. I was not part of the review for this adverse outcome pathway.
MS. KING: Do you have another copy? Is that going to be the case with all of the exhibits? Because I'm going to want a copy so I can look at it all along.
Depending on how we go, I might need to ask for a break and get a copy made.
MR. MURDICA: You know what, we'll --

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MS. KING: Go ahead.
MR. MURDICA: We'll come back to it, that way you have -- you have your own copy --
MS. KING: Thank you.
MR. MURDICA: -- when we do.
QUESTIONS BY MR. MURDICA:
Q. Let's go back to genetics. We'll come back to this later.
In your -- in your practice, do you treat any human patients?
A. Treat, we do not -- I do not treat patients.
Q. Okay. You do not diagnose patients, correct?
A. I do genetic analysis consistent with identifying mutations in human patients, but I'm not allowed to diagnose patients.
Q. And that's -- is that because you're not a medical doctor?
A. It's because I'm not a licensed geneticist or medical doctor or medical geneticist.
Q. In your rebuttal report, you

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reference Dr. Chung many times.
Do you know Dr. Chung?
A. Not personally.
Q. Okay. Have you ever interacted with Dr. Chung in any way?
A. Not personally.
Q. Okay. Is there any reason why you would like or dislike Dr. Chung personally?
A. No.
Q. When you compared Dr. Chung to defending war criminals, that wasn't from any personal opinion?
MR. TRACEY: Object to the form.
THE WITNESS: I was referring to the drugs as -- and the fact that they were human teratogens, that they were similar to war criminals in the fact that they had maimed and hurt people, the chemicals.
QUESTIONS BY MR. MURDICA:
Q. Is that -- is accusing people of defending war criminals something that you -- is that the way you talk in your

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normal work outside of litigation?
A. If it's in regards to teratogens that can have a detrimental effect on people, I reckon everyone's entitled to a defense in our -- in our country, but nevertheless, those compounds are particularly dangerous.
Q. Right.
And what Dr. Chung was talking about was whether or not they induce autism, not whether or not they're dangerous or induce major congenital malformations, correct?
A. Compounds that can cause congenital malformations and autism are dangerous compounds.
Q. Yeah, and that's not -- that's not what I was asking.
You realize the portion of Dr. Chung's opinion that you were criticizing was about whether those compounds cause autism and other effects, not whether they cause major congenital malformations, correct?
A. Well, as autism is represented

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as a functional deficit that is correlated with congenital malformations, specifically like neural tube defects, those are similar in that regard.
Q. Is autism a structural birth defect?
A. That's -- it's diagnosed by behavioral testing clinically.
Q. Right.
So it's not diagnosed as a structural birth defect, correct?
A. There are structural defects associated with it, but it's not part of its diagnosis.
Q. Okay. And not every -- not every compound that induces structural birth defects also induce autism, correct?
A. That is correct.
Q. Okay. In fact, of the -- of the antiepileptic drugs -- of which you believe many cause major congenital malformations, correct?
A. That's correct.
Q. Only one has been associated with autism to date, correct?

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A. We're currently conducting those studies in animal models, but in the -- as far as the handbook for physicians, it was specific to valproic acid.
Q. Okay. Are there other antiepileptics that you believe cause autism?
A. We're currently looking at that.
Q. Okay. Are there any that you believe so far cause autism?
A. We're still blinded to that data, and I'm not ready to draw conclusions on it.
Q. Okay. And when you say "we," you're doing more animal studies on antiepileptics?
A. Yes, we are.
Q. Which antiepileptics are included in your studies?
A. Well, valproic acid, in addition to -- and I don't have them all in front of me, but there's several other compounds that we're testing that are also anticonvulsant drugs.
Q. Okay. But you can't think of

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any of them?
A. Not just the top of my head. I have to have the grant in front of me to tell you which one of the compounds we're looking at.
Q. Okay. Are you doing that at Baylor?
A. Yes, we are.
Q. And who is funding that?
A. Right now, it's not funded.
Q. Is that -- what portion of the work you're doing now in -- at Baylor is that, is antiepileptic animal studies?
A. I've only had one grant funded in antiepileptic drugs, even though we've studied it for decades, and none of our funded work right now is in anticonvulsant drugs.
Q. Okay. What is your funded work now?
A. In anti -- the HIV antivirals.
Q. Oh, it's what we've talked about before?
A. Yes.
Q. Is that the majority of your

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time right now?
A. Yes.
Q. Understanding that you -- I think you said you can't -- even though you can conduct genetic testing, you can't diagnose anyone; is that right? You can't diagnose a human patient?
A. Yes. So we run human patients for what's referred to as sequencing or resequencing. We also can send out for whole genome, and I do the analysis of that, but I provide the reports back to whomever is the intended physician or the medical geneticist for diagnosis.
Q. Okay. And I assume you've never diagnosed anyone with autism or ADHD. Is that fair?
A. We've had patients that have mutations that were consistent with autism that we identified in our laboratory.
Q. Okay. And you, Dr. Cabrera, never diagnosed a patient with autism or ADHD, correct?
A. I don't do diagnosis for autism.

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Q. Okay.
A. But the patient herself was -- did have autism.
Q. Do you know the diagnostic criteria to diagnose a patient with autism?
A. I'm familiar with the DSM for diagnostic, but I'm not -- haven't performed the test, nor am I licensed to do such.
Q. Okay. What are the -- what are the diagnostic criteria for autism?
A. So typically it's -- has to do with focus and attention, repetitive behavior and then social communication disorder.
Q. And do you know to what extent any or all of those need -- boxes need to be checked in order to render an autism diagnosis?
A. There's a score system that's based on that, and -- again, I'm not a diagnostician in that regard. And then the last one is that they should have a negative effect on the person that has autism. And so meeting all those criteria is enough to create the diagnosis. But I -- I'm not familiar with the scoring because I don't do

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that in my -- in my regular work.
Q. Okay. What do you mean by "negative effect"?
A. That it has a detrimental effect on the well-being of the person.
Q. Okay. So if somebody is a savant, is that a detrimental effect?
A. Well, if it has negative effects on them otherwise, as far as social and communication, then that could be an indication of that.
Q. Okay. And if I asked you the same questions with regard to ADHD, would you give me the same answers; in that you don't know the exact criteria and you don't diagnose?
A. I don't do the diagnostics for ADHD.
Q. And you don't know the diagnostic criteria exactly, correct?
A. Outside of what's in the DSM, I have not and never plan on performing those tests.
Q. Okay. And you just testified about genetic changes that you thought were

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consistent with autism.
Was that following whole-exome sequencing?
A. We did perform whole-exome sequencing on that -- on that individual.
Q. Okay. And you've seen -- have you seen point mutations that you thought were consistent with autism?
A. In this particular case, we saw a mutation that was in a particular gene that we then produced a mouse model for, and the mouse model displayed behaviors also that were consistent with autism. And so collectively, we reported that this gene was associated with core behaviors in the mouse and would be specific for this human.
And then another colleague at Baylor identified multiple other patients with the same mutation, the same gene with similar presentation.
Q. And there's multiple mutations that have been identified in patients with autism, correct?
A. That is correct.
Q. And is there any consistent

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pattern of mutations that's known for autistic patients at this point?
A. There are some major genes that have been associated with autism, and there are also other minor genes that have been shown to interact with the autism risk.
Q. Right.
And interaction itself, it's still wide open, right, as to what actually causes autism genetically, in your mind?
A. Well, it depends on the particular case.
Q. Right.
It's not a -- it's not a uniform presentation genetically, even for genetically caused autism, correct?
A. It depends on the case.
Q. Okay. Well, did autism exist before pharmaceutical compounds existed?
A. As far as I know, yes.
Q. Okay. There's autism documented back in ancient Egypt, right?
A. I'm not familiar with that record. I'd like to see that document.
Q. Okay. When do you first know

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of autism being diagnosed in human beings? Not diagnosed.
When do you first know of autism symptoms being observed in human beings, in the human record?
A. Well, consistent with a clinical diagnosis, I was only following the literature since probably the -- me personally, since the DSMs had been in development and listed autism and infantile autism as particular outcomes.
Prior to that, there are behaviors consistent with what we now think of as autism but not a clinical diagnosis of autism.
Q. And when you were following -- so how long has that been that you've had some awareness of autism?
A. Since -- I think since I was being trained in teratology.
Q. Okay. And since you were being trained in teratology, had you ever looked into thimerosal as a cause of autism?
A. I did look at heavy metals and particularly thimerosal as well.

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Q. Okay. And sitting here today, do you believe that thimerosal causes autism?
A. Not thimerosal as a particular compound, but mercury, as a causative agent, is associated with the same endpoints that are identified in AOP 20.
Q. Right.
So do you believe -- do you believe that mercury induces autism?
A. I believe that mercury can increase the risk for autism, yes.
Q. So mercury can cause autism in a particular patient, correct, in your view?
A. Depending on the exposure, it's been shown that mercury exposure can increase the risk for autism.
Q. Okay. Can --
A. And that is causative in regards to the AOP.
Q. Okay. Can -- so the AOP itself is enough for you to determine causation in that instance?
A. It's not enough to determine causation, but it's enough to demonstrate molecular interactions that can produce a

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presentation based on biological structure.
Q. And then you, Dr. Cabrera, make the additional leap and say that it's causative, correct?
A. There -- there's no leap there. Then you would apply Bradford Hill in order to determine whether there's a -- there's causality.
Q. So you, Dr. Cabrera, then apply Bradford Hill as you see it and determine causality, correct?
A. So -- well, you systematically review the literature and see if -- how the different factors in regards to Bradford Hill support causality or not.
Q. And you've done that for mercury and determined that it's causative, correct?
A. I've looked at that for mercury.
Q. Okay. Have you looked at it for thimerosal?
A. Not as thimerosal as a, you know, derivative of a mercury-containing compound, no.

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Q. Sitting here today, do you believe that thimerosal causes autism?
A. I haven't looked at it in detail enough to know that.
Q. Okay. Can you exclude it as a cause of autism?
A. I would say that there's -- in regards to vaccination, that that literature has not supported thimerosal specifically as a -- as a cause.
Q. Did you ever look at all the thimerosal vaccine literature?
A. Yes, I did.
Q. Okay. And did you look at it prior to that being debunked?
A. Concurrently.
Q. Concurrently.
So you didn't look at it before it was debunked, correct?
A. Well, I was familiar with the study when it came out, and then with, would you say, this controversy surrounding how the study was conducted, and then the aftermath of that. I was familiar with all that, yes.
Q. Okay. So you know that there

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were something like 14 studies that initially indicated that thimerosal might induce autism via vaccination, correct?
A. I'm -- I don't know what the count is on that.
Q. Okay. But you know that at some point there were a whole bunch of studies, whatever number, that people -- some scientists believed indicated that thimerosal could cause autism, correct?
A. I'm familiar with of that.
Q. Okay. And at the time you hadn't looked at those, right?
A. At the time?
Q. At -- well, when they were only those studies that had some people, some scientists, some plaintiffs' lawyers, believing that thimerosal could induce autism, you hadn't looked at those, right?
A. I was familiar with the literature --
MR. TRACEY: Objection to the form.
THE WITNESS: I was familiar with the literature supporting that

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position.
QUESTIONS BY MR. MURDICA:
Q. Okay. And did you believe at the time that thimerosal could cause autism?
A. Well, I was familiar with the fact that mercury could produce neurotoxicity and neurodevelopmental toxicity, but I wasn't -- specific in regards to thimerosal, I wasn't -- I hadn't drawn any conclusions in regard to -- specifically to thimerosal.
Q. Okay. And you know that since then, it's the unanimous opinion of scientists that thimerosal does not cause autism, correct?
A. I don't know about the unanimous decision, but I can say it's generally accepted.
Q. Okay. And do you accept that, Dr. Cabrera?
A. I think that it's still unclear in regards to the effects that mercury can have. And I know people know now that they've removed it out of all of the vaccines, but there's not going to be any more data on that.

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So it's still open, and I don't think it'll be ever closed completely.
Q. Do you consider yourself an anti-vaxxer?
A. I do not.
Q. Okay. You accept the science as it comes, right?
A. I weigh it as I'm trained to do.
Q. Okay. Does maternal fever cause autism?
A. Maternal fever can also increase the risk for autism.
Q. Okay. So you keep saying "increase the risk," when I say "cause."
Here, you're proposing to tell the world that acetaminophen can cause autism, correct?
A. Well, I've conducted an analysis consistent with causality for acetaminophen. I haven't done the same analysis for fever, but I'm familiar with the literature on fever increasing the risk for autism, and that can be consistent with a causal effect.

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Q. Okay. And you realize that many of the patients that are pregnant that take acetaminophen have maternal fever and that's why they take it, right? That's one of the indications?
A. I think it's a compound question, but one of the indications for acetaminophen is -- taking acetaminophen is fever.
Q. Right.
But yet, you haven't done a full study of fever as a causative agent -- as a causative exposure for autism, correct?
A. I have a proposal to do that, but we have not --
Q. And where is that proposal?
A. On my computer.
Q. Okay. I mean --
A. I've sent it off once. I'm going to be resubmitting that for funding.
Q. Okay. And I guess that's what I was asking.
So it's a proposal to get funding to, what, the NIH or something like that?

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A. Yeah. So when I was in graduate school, we did increase in maternal body temperature as another model for neural tube defects and showed that fever can produce neural tube defects, and I would like to follow up that work with the effect of fever on autism as an outcome.
Q. Okay. In Dr. Cabrera's view, what else are you -- what other exposures, if any, are you convinced can cause autism?
A. Things that's supported in the literature, fever would be one of them, in addition to heavy metals such as mercury. And there's also -- and I'd say that the data, at least at this point, is insufficient but supportive of -- would be small particle, air pollution particularly, benzopyrene and some industrial compounds in that -- in those particles.
Q. Okay. And have you looked at any of those in the context of litigation?
A. I have not. Well, some heavy metals I have, but not in regards to autism.
Q. Okay. In regards to autism or ADHD, have you looked at any other

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environmental exposures outside of the context of litigation?
A. I have not.
MR. WATTS: Hey, Jim, we've been going about an hour.
MR. MURDICA: Yeah.
MR. WATTS: First break?
MR. MURDICA: Sure, that's fine.
VIDEOGRAPHER: Off the record, 10:01.
(Off the record at 10:01 a.m.)
VIDEOGRAPHER: The time is 10:22, back on the record. Beginning of Media 2.
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Cabrera, are you ready to proceed?
A. I am.
Q. Okay. I'm going to ask you some questions about basics of statistics in reviewing some of the articles that are part of your report.
Dr. Cabrera, do you believe that results need to be statistically

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significant to be meaningful?
A. Not necessarily.
Q. Okay. Are you part of a group supporting abandonment of statistical significance in epidemiology?
A. Not abandonment, but just clarification inasmuch as when those statistics were introduced, they weren't introduced for the -- for the kind of line in the sand that has been drawn with them. That was not their intention when they were introduced.
Q. Okay. In your opinions here, in forming a causation opinion, are you relying for causation on any results that did not achieve statistical significance?
A. I'm relying on the totality of evidence, and some of that did not achieve statistical significance.
Q. Okay. And just so we understand, statistical significance would be where a result finds an odds ratio or a relative risk that does not include the null, correct?
A. The confidence interval that

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doesn't include the null typically.
Q. Okay. And conversely -- so that could be a finding that's significant that shows an effect, right? Because it's over 1 in the -- in both ends of the confidence interval, correct?
A. To clarify, you can have an increase in risk, and that would be greater than 1, or a decrease in risk, and that would be less than 1 --
Q. Right.
A. -- as far as the point estimate.
Q. And if the confidence interval and the point estimate are all less than 1, that is a decrease in risk, correct?
A. That can be interpreted as a decrease in risk.
Q. And it could be interpreted as whatever that exposure is is protective against whatever the effect is, correct?
A. So, yeah. I mean, effectively it's whether you're accepting or rejecting a null hypothesis. In that case, you can say, you know, we're not accepting, we're

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rejecting.
Q. Right.
And if an exposure has a point estimate and a confidence interval that's entirely under 1, in that study, in that population, it would be -- it would show a protectiveness of that exposure to the end effect, correct?
A. A decrease in risk.
Q. Okay. Sure.
P-value, what does a p-value need to be to be meaningful to you, Dr. Cabrera?
A. So p-values generally would be set as a -- as a function of whatever analysis you're doing, preferably before you conduct the analysis. And most commonly, it's the -- the alpha set it to -- it's referred to a 0.05. So it's a 5 percent false discovery.
Q. Right.
That's the statistical convention that most people use, correct?
A. Depending on the type of analysis you're doing. In some cases it may

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be lowered depending on the type of analysis you're doing.
Q. You've seen p-values that come out to be .00001, right?
A. Yes, I have.
Q. And that would be more meaningful to you than .05, wouldn't it?
A. It's not a more meaningful. It's just in regards to whether we're looking that as a -- as part of our false discovery, or you're not liable to find that as part of your false discovery.
Q. And as part of false discovery, if your p-value is .1, that would be an increased chance that you made a false discovery, correct?
A. Yeah, you -- it's correct.
Q. .1 -- by convention, .1 wouldn't be a very good p-value, right?
A. Passing judgment, if you set out in your statistical testing to set it at something less than 0.05, generally you would need to justify that, why you're setting that at .1, so it would depend on the analysis you're doing.

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Q. Okay, sure.
But that wouldn't -- that wouldn't be a result that would be very exciting to you based on statistical convention, correct?
A. Depending on the analysis I'm doing, but generally speaking, particularly with tests that you haven't run before, you would start out with an alpha of 0.05.
Q. Okay. I'm going to ask you some questions about SSRIs.
Dr. Cabrera, do you believe sitting here today that SSRIs cause autism?
A. I haven't looked in the literature in regards to the SSRIs and autism.
Q. Do you believe that SSRIs cause ADHD?
A. I haven't looked in the literature with regards to SSRIs and ADHD.
Q. Okay. Did you ever work out -- did you ever work on SSRIs at Baylor?
A. I -- we -- I believe we did publish a paper. I'm not sure if it was while we were at Baylor or just before we

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came to Baylor on SSRIs.
Q. Okay.
A. Particularly sertraline.
Q. I'm sorry?
A. Particularly sertraline.
Q. Oh, sertraline.
A. Yes.
Q. Got it. Got it.
And do you recall what the conclusion was of your research or your paper?
A. Yes. We found that it had a teratogenic effect. Specifically we found clefting in the animals.
Q. And that was a paper right when you started your work at Baylor?
A. Yeah, it coincided -- I'm not sure if we published that while we were at Baylor or while we were at UT, just before we left. I would have to look at specifically when we published that.
Q. Got it.
In the context of litigation, have you ever worked on SSRIs?
A. Yes, I have.

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Q. Okay. And when was that?
A. It's on my CV. I don't have the exact year.
Q. Okay.
A. It's been several years.
Q. Did you draw any conclusions in the context of litigation regarding SSRIs?
A. Yes. We were looking at outcomes for developmental toxicity and particularly impacts on congenital malformations.
Q. Okay. And that was for litigation, right?
A. Yes.
Q. And was that for lawyers based in Houston?
A. In part.
Q. Okay. Was that for Mr. Tracey?
A. In part.
Q. And what did you conclude in that litigation? Did you find a relationship between SSRIs and developmental outcomes?
A. We did find support for that, yes.
Q. And did you render an opinion

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that SSRIs cause developmental issues?
A. Yes, I did.
Q. And what issues did you say SSRIs caused?
A. At the time the major congenital malformation that was of interest was congenital heart defects.
Q. In the context of litigation, have you evaluated any other exposures and developmental outcomes?
A. Can you repeat the question?
Q. Sure. No problem. We had a little unexpected phone call there.
In the context of litigation, outside of your regular work --
A. Uh-huh.
Q. -- have you evaluated any other exposures and developmental outcomes?
A. Yes.
Q. And what are those?
A. Largely occupational exposures and environmental exposures.
Q. Okay. Have you -- have you ever done work in the context of litigation on the drug Paxil?

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A. Yes, I have.
Q. And that was also for plaintiffs' lawyers in Houston, correct?
A. That's correct.
Q. Okay. Was your work on Paxil the first work that you did with plaintiffs' lawyers?
A. I believe the first work we did was with sertraline.
Q. Okay. And it's all been in part with the same firm that we're sitting in now, the Tracey law firm, correct?
A. No, it's not correct.
Q. Okay. What other firms has it been with?
A. I've also worked with some other firms in our area and then also in Colorado as well.
Q. Okay. And which firms are those?
A. Here, Clark -- Clark Love Hutson.
Q. Uh-huh.
A. And in Colorado, I would have to get the particular firm name. It's --

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Q. All right. I'll ask you again in case you remember it.
A. Yeah. Pozner. Maybe Pozner, Pozner.
Q. Oh, yes. Reilly -- Reilly Pozner.
A. Yeah.
Q. Or Pozner Reilly. Yeah, okay.
Dr. Cabrera, do you know if your opinion on SSRIs -- you said SSRIs cause developmental defects, correct?
A. Yes.
Q. And was that opinion accepted in court?
A. As far as --
MR. TRACEY: Objection. Form.
Go ahead. You can answer, Robert.
THE WITNESS: As far as my opinion, it's -- there was -- accepted. I think there was also some -- also another expert was rejected, and so overall, that was not accepted.

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QUESTIONS BY MR. MURDICA:
Q. You have an understanding that you were excluded as -- you were not determined to be a qualified expert. You were excluded from that litigation, correct?
A. I was qualified as an expert, but my understanding is that based on the exclusion of the epidemiologist, the case didn't move forward.
Q. Do you know you were excluded as an expert?
A. I think collectively because of the exclusion of the epidemiologist, we were excluded.
Q. Okay. So you don't deny that you were excluded as an expert in SSRI litigation, correct?
MR. TRACEY: Object to the form.
THE WITNESS: Yeah. To be clear, there were some criticisms rendered in regards to my opinion, but my understanding is that the exclusion was based on the rejection of the epidemiologist.

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QUESTIONS BY MR. MURDICA:
Q. Have you ever seen the opinion?
A. I've read it.
Q. When's the last time you read it?
A. It's been several years.
Q. Okay. We'll take a look at it later.
In Paxil, what opinion did you render there?
A. That it could also increase the risk of adverse outcome in -- with in utero exposure.
Q. Okay. So to be clear, plaintiffs' lawyers hired you in Paxil litigation, and you offered an opinion that Paxil could cause developmental defects, correct?
A. That's correct.
Q. Okay. Did you ever testify in court on that?
A. I did not.
Q. Do you know if your opinion -- did you ever testify at a deposition about that?

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A. Yes, I did.
Q. Okay. Do you have a copy of that transcript?
A. I do not.
Q. Do you generally -- when you do work for plaintiffs' lawyers, do you get copies of the transcripts afterwards?
A. Sometimes. Not always.
Q. Okay. Do you keep them?
A. From that long ago, I wouldn't still have it.
Q. Okay. How about from SSRIs, do you have those transcripts?
A. I do not think I have any of those S -- SSRI transcripts.
Q. Okay. When is the last time you testified at deposition before today?
A. My last depositions were just in the last few years. I've given some depositions.
Q. Okay.
A. But not on SSRIs.
Q. Were they on -- were they in litigation?
A. Yes.

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Q. Were they on environmental exposures?
A. And occupational -- environmental and occupational exposures.
Q. Okay. And in each of those instances where you gave a deposition, were you being paid by the plaintiffs' attorney?
A. Yes, I was.
Q. And is that the case going back all the way to Paxil, that whenever you've given a deposition rendering an opinion about an exposure, it has been for a plaintiff's attorney?
A. That is correct.
Q. And in each of those, when you've given a deposition being paid by a plaintiff's attorney, you've always come to the conclusion that the exposure caused a defect, correct?
A. To be clear, in the cases I reviewed where I didn't support that opinion, I haven't been deposed on them.
Q. Well, let me -- let me ask again because I understand what you're saying, but I want to get a clear answer on

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this one.
Every time that you've been deposed in litigation, it has been when you've been paid by a plaintiff's attorney and when you've come to the conclusion that the exposure caused the -- a defect in a human being, correct?
A. So I've been paid by plaintiffs' attorneys to offer my opinion. When I found that there wasn't evidence enough, I've never been deposed about that opinion.
Other times, I have been deposed, and in those cases, they were plaintiff opinions or opinions that I submitted because I was asked to by a plaintiff attorney.
Q. Do you remember my question?
A. Yes.
Q. What was it?
A. You were asking me if I had ever rendered an opinion asked by plaintiffs' attorneys to -- if all of the opinions that I rendered were asked for by plaintiffs' attorneys.

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Q. My question was, every time that you've been deposed in litigation, it has been in an instance where you're being paid by a plaintiff's attorney and where you've rendered an opinion that the exposure caused an outcome of a defect in a human being, correct?

A. So -- and I'm just clarifying that.

Q. Is that a "yes" or a "no"?

A. Well, my clarification is I have rendered those opinions, and the ones that were at deposition, I was paid by a plaintiff's attorney.

But I've also been asked to render opinions, and when I found that there wasn't evidence, then I didn't go to deposition. I wasn't asked to provide a deposition in that regard.

Q. Okay. And do you have any proof of any kind that you've rendered opinions finding a lack of a causal connection between an exposure and a -- an outcome in a human being where you haven't gone to deposition?

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A. Regular conversations --

MR. TRACEY: Objection to form.

THE WITNESS: Regular conversations I have with -- when I am consulting, right.

QUESTIONS BY MR. MURDICA:

Q. There's nothing you can show me or the Court here that that's ever actually happened, right?

A. Well, it's confidential, so I can't -- I can't --

MR. TRACEY: Yeah, Robert. Be careful about confidentiality, Robert.

QUESTIONS BY MR. MURDICA:

Q. Yeah. I just want to be clear for the record, for the Court, because that's who's ultimately going to read this.

Sitting here today, there's nothing you could show the Court to verify what you just said about ever opining other than the exposure caused the defect, correct?

MR. TRACEY: So, Robert, hold on. I want you to be careful about that question, because if there exists evidence that satisfies that question,

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that is, if there is evidence where you have told lawyers that they don't have a case, but that is confidential, that exists, but you may not be able to disclose it.

Are you with me?

THE WITNESS: Yes, and that's what I've conveyed. I can't disclose that.

QUESTIONS BY MR. MURDICA:

Q. Okay. And I'm just saying, there's nothing you can disclose to show that you've ever rendered an opinion other than the exposure caused the defect for a plaintiff's attorney, correct?

MR. TRACEY: Well, no, object to the form. It's other than confidential information.

MR. MURDICA: Okay. I will ask it again, Mr. Tracey.

QUESTIONS BY MR. MURDICA:

Q. Is it your testimony that you have confidential information that you would be able to show if it wasn't confidential and that we may be able to get a Court to protect

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or maybe you could provide to the Court directly to show that you've ever rendered an opinion for a plaintiff's attorney other than one that supported their theory that an exposure caused an outcome in a human being?

A. Yes, I have. I provided that opinion confidentially before.

Q. Okay. And you have proof of that. You -- it's just -- you just can't show it to us because it's confidential, correct?

A. I could produce proof of that, but it's confidential.

Q. Okay. For the stuff that we are able to discover and that the Court can see, you've always sided with the plaintiff when it comes to an exposure and an adverse outcome in a human being in litigation, correct?

A. To be clear, I've only been asked by plaintiffs' attorneys to render opinions in the past.

Q. Okay. And when you do that kind of work for plaintiffs' attorneys, do you seek the permission of UT or Baylor to do

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it?
A. I have not. I consult independently for that.
Q. Okay. Do you know if Baylor or UT have a policy about work outside of the universities?
A. I'm required to file conflict of interest.
Q. Okay. And you did so here, I assume?
A. I've filed a conflict of interest with my company.
Q. What does that mean, with your company?
A. So my -- I file a conflict of interest under my company with Baylor.
Q. Okay. So Baylor does know that you are testifying against the entire industry of manufacturers of acetaminophen, correct?
A. Baylor knows that I work for a consulting company --
MR. TRACEY: Object to form.
THE WITNESS: -- that is working in litigation, not the

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specific cases.
QUESTIONS BY MR. MURDICA:
Q. So they don't know your actual opinion here, correct?
A. They do not.
Q. Okay. Have you shared your opinion here with anyone other than the plaintiffs' attorneys and anyone that they've given your reports to?
A. Yes, I have.
Q. Who is that?
A. My laboratory.
Q. Okay. Outside of your laboratory, have you shared it with anyone else?
A. My wife.
Q. Okay. Outside of a personal relationship, have you shared it with anyone else?
A. Outside of my laboratory and personal relationships, I have not.
Q. You haven't, for example, contacted any of the scientists involved in the studies that are contained in your report, have you?

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A. I have had some Zoom interactions with other experts in this regard, but not with any other scientists in the literature.
Q. Okay. And by other experts, you mean other hired experts by plaintiffs?
A. That's correct.
Q. Okay. Outside of hired experts by plaintiffs, have you discussed your opinions that we're -- that we're talking about today with any other scientist outside of your lab or outside of hired experts?
A. And outside of personal?
Q. Right.
A. I have not.
Q. Okay. Have you contacted any regulatory authorities or Teratology Society or Maternal-Fetal Medicine or American College of Obstetricians about your opinions?
A. I've spoke with an obstetrician in our laboratory, but outside of that, no.
Q. Do you think it's important that maternal fever is treated during pregnancy?
A. It is important.

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Q. Okay. Why is it important?
A. Because fevers have adverse outcomes during pregnancy if they're not controlled.
Q. Do they have adverse outcomes for the fetus?
A. Yes, they can.
Q. And what adverse outcomes can those be?
A. Fevers can increase risk for congenital malformations specifically. It's been widely published in the literature and also supported in animal models.
Q. And I think you testified earlier that fevers can cause autism, correct?
A. That is correct.
Q. And fevers can cause ADHD?
A. There are studies that support that, yes.
Q. Okay. And you don't dispute it, do you?
A. I'm not disputing that fevers are dangerous, particularly for --
Q. Okay.

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A. -- anyone to have a fever or too high of a fever or particularly for pregnant women to have a high fever for a prolonged period of time is dangerous --
Q. What --
A. -- for the mother and the fetus or the embryo.
Q. What other antipyretics would -- what could treat fever in a pregnant woman that's available on the market right now?
A. It depends on when the medication is taken. There are different contraindications for other antipyretics.
Q. Okay. How about opioids, do you think women should treat fever with opioids?
A. I don't think opioids would be a good way to treat fevers.
Q. Why not?
A. Well, one, they're known to be addictive. That's a potential problem with an opioid use, particularly with a pregnant mother.
Q. Okay. When you just testified

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a minute ago about talking to the other plaintiffs' experts in this litigation, I have a couple of questions about that.
When was the last time --
MR. TRACEY: Wait. Wait. Wait. Wait.
Jim, I thought we had an agreement that we weren't going to talk about that.
MR. MURDICA: About experts talking to experts? I'll look at our agreement. I thought it was about lawyers.
MR. TRACEY: I thought it was any communication -- well, so, I was there, so it's kind of hard to tease it out.
MR. MURDICA: All right. I'll think about that and move on.
MR. TRACEY: Okay. Okay.
(Cabrera Exhibit 2 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Can I have the rebuttal report? Or did you bring your reports?

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A. I brought a rebuttal report. I do have my rebuttal report.
Q. You have your rebuttal report?
A. Yes.
Q. Well, I'll mark a copy so you can go with an exhibit copy.
Dr. Cabrera, you now have in front of you Exhibit 2, which is titled your rebuttal report.
Do you see it?
A. Yes, I do.
Q. Does that look like your rebuttal report?
A. It does.
Q. Okay. Is this the last report in writing that you've rendered with regard to this litigation?
A. Yes, it is.
Q. Okay. Right as we started the deposition today, your counsel handed me a stack of articles.
Were those provided by you?
A. Yes, they were.
Q. Okay. And those were since the rebuttal report, correct?

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A. Yes.
Q. Okay. And that you first reviewed them since the rebuttal report?
A. Concurrently. I hadn't included them in the rebuttal report when I was reading through the literature, and I believe one of your criteria was that I provide all the information that I had reviewed in my opinion, but they aren't specifically referenced, but I was provided.
Q. Okay. Some of the studies are not -- one of the studies is from this week, right?
A. Yes.
Q. Okay. But the rest of them are from 30, 20, 15 years ago, correct?
A. They vary, yes.
Q. There's no reason you couldn't have found those before your rebuttal report, correct?
A. Oh, it wasn't a matter of finding them. I had found them. They were just still open on my browser, and I felt it appropriate that I send them all to counsel because I had reviewed them.

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Q. Okay. Are they referenced in your rebuttal report or your other report?
A. They're references in regard to some of the other expert's opinion that were provided that I hadn't had a chance to include in my report.
Q. Okay. So if we looked in your reports, we wouldn't see the citations to the new articles that were handed to me this morning, correct?
A. I do not think you would see them, no.
Q. Okay. And your testimony is that you wanted to make sure we had everything you ever looked at, even if you didn't reference it, correct?
A. Well, because I was looking at it in response to the expert reports that were provided to me that are appropriate, that I provide all of the reports that I did look at.
Q. Okay. So now we can be comfortable that we -- between your reliance list and everything I was handed this morning, we have everything you looked at,

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considered in rendering this, correct?
A. Well, I looked at some other stuff last night as well, but --
Q. Okay. What did you look at last night?
A. A couple of studies that were -- I did print them out, but I haven't sent them for counsel yet.
Q. Okay. Do you have those with you?
A. I do.
Q. All right. Can I have them, please?
MR. TRACEY: Can we, excuse me, identify them on the record?
MR. MURDICA: Yeah, I'll identify them.
MR. TRACEY: Okay.
MR. MURDICA: Dr. Cabrera just handed me a paper from 2015 called Biochimica et Biophysica Acta. That's the journal article. "Glutathione during embryonic development."
We'll get copies and mark them later.

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QUESTIONS BY MR. MURDICA:
Q. Anything else, Doctor? Oh, you have a whole stack?
A. No, just this. Just these two.
Q. And the paper on oxidative stress from 2019 by an author called Moore.
Okay. With those two papers, Dr. Cabrera, can we be satisfied that we have everything you relied on up to this point today?
A. I think so, yes.
Q. Okay.
All right. Is there anything about Exhibit 2, your supplement report -- supplemental report, that you don't stand by, that you need to change, that you need to revise, that you need to withdraw, sitting here right now?
A. No.
Q. Okay. All right. If you turn to the last page of Exhibit 2, that's your signature, right?
A. Yes.
Q. This is your report?

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A. Yes, it is.
Q. Okay. So first thing I want to ask you about is on page 5.
In your supplemental report, for the first time you list genes that you say, quote, "interact with acetaminophen."
Correct?
A. That's correct.
Q. Okay. And you start talking about catechol-O-methyltransferase, right?
A. That is listed there, yes.
Q. And I'm going to butcher the pronunciation because I don't know this one. Capicua?
A. Capicua.
Q. Capicua?
A. Yes.
Q. And capicua is something that you've studied in at least one study in your lab, or that Finnell has in his lab, correct?
A. Yes, it's one thing we've studied in the group.
Q. And you say here in your supplemental report that capicua interacts with acetaminophen in a study of

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acetaminophen toxicity. And you say that on page 5, correct?
A. Just to be clear, I do report that on a multicenter study that was based on murine hepatotoxicity that they looked at this interaction.
Q. I'm looking at the sentence "CIC" --
Which is capicua, right?
A. Yes.
Q. -- "was reported to interact with acetaminophen in a multicenter study of acetaminophen toxicity."
Right?
A. That's correct.
Q. And then you cite Beyer.
A. Yes.
Q. Okay. Can we mark this, please?
(Cabrera Exhibit 3 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Cabrera, I marked as Exhibit 3 is -- well, you tell me what it is.
A. This is a report by first

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author Beyer titled "Multicenter study of acetaminophen hepatotoxicity reveals the importance of biological endpoints in genomic analysis."
Q. Okay. And is this what you cited as footnote 15?
A. Yes.
Q. Okay. Could you show me where in this exhibit it says that capicua interacts with acetaminophen?
A. I think it's actually in the data, in the dataset.
Q. Okay. And where is the dataset?
A. Online. It's in the dataset here.
Q. Okay. If we look in the article, it won't say it anywhere, right?
A. No, it's actually in the data.
Q. Okay. When is the last time you looked at the data?
A. When I wrote the report.
Q. Okay. So three weeks ago, a month ago?
A. Yes.

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Q. Something like that?
And this is about -- this Exhibit 3 is about hepatotoxicity, which is liver, correct?
A. It is about hepatotoxicity, which I do indicate in the report.
Q. And this capicua is not mentioned in your initial or amended reports, only in your rebuttal report, correct?
A. That is correct.
Q. How many other genes, if you remember, were mentioned in that -- in the data supplement to this article?
A. I would have to go through and count them, but several.
Q. Several or a lot?
A. Several other genes. I don't know -- what is a lot?
Q. Well, hundreds? Tens?
A. Not hundreds.
Q. Okay.
A. They're -- in regards to gene interactions, I did report that there were 273 genes that were reported to interact with acetaminophen in ASD, and that's from the

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database, which I previously cited in my first report.
Q. Right.
Okay. Let's talk about that database.
Who hosts that database?
A. I'd have to look back. Maybe in North Carolina, or one of the Carolinas. I'll have to look back specifically at the study.
Q. Right.
And what databases are available, other than that database, if you want to do this type of research on genes and interactions?
A. There are numerous databases for looking at these types of interactions.
Q. Okay. What databases do geneticists generally rely on?
A. Typically, most geneticists, and what I teach the geneticists because I also cover this in my lectures for genetic counselors, is the use of, like, the Online Mendelian Inheritance in Man. And not a specific endorsement, but that would be one.

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Q. OMIM?
A. Yes, referred to as OMIM.
Q. How about SFARI?
A. As far as autism genes, it's a database that's also used.
Q. SFARI is?
A. Yes.
Q. Right.
Okay. How about ClinGen?
A. It is another database that's used, yes.
Q. Okay. This one that you cite is not one that's commonly used, correct?
A. This is a database for archiving molecular interactions, where those are more specific to genetics and the presentation of various gene pathologies.
Q. Okay. And when you went -- when is the last time you went into this database? Was it when you did this rebuttal report?
A. That is correct.
Q. Okay. Well, I'll ask you if you remember; but if not, we'll take a look at it.

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Do you know what the criteria is for a gene to become part of these 273 genes that you report interact with acetaminophen?
A. They're -- if they're listed as changing an expression in the database or physically interacting -- there are different criteria in the database that are identified, and you can specify what criteria you want to use.
Q. It's changing any expression, right, at all?
A. You can select whether it's up or down or an interaction.
Q. And when you get to the page where the 273 genes are listed, there's a link where you can look at the backup for that, right?
A. Yes, you can.
Q. Did you do that?
A. Yes, I did.
Q. Okay. Did you see that one of the 273, the vast majority of them, were in one study, one paper?
A. Generally, they derive from

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particular studies using expression data. So a lot of it do come from individual studies.
Q. Okay. And did you look at the -- did you know that, that 200-and-something of the 273 all come from one study?
A. I was aware of that.
Q. Okay. And did you look at that study?
A. I did.
Q. Okay. And did you see acetaminophen in that study?
A. Might have to go back and look at it specifically and what the different exposures were.
Q. Okay. Is it your understanding that that study that included more than 200 genes that are attributed here connected acetaminophen and autism with those genes?
A. The -- this is a data risk report in regards to those that were associated with ASD and acetaminophen exposure. So that is consistent with what I found in the database.
MR. MURDICA: We'll mark this

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as Exhibit 4, please.
(Cabrera Exhibit 4 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, you have in front of you Exhibit 4, which is an article by Santos.
Now, if you recall, this is the one that's attributed -- to which is attributed more than 200 of those genes. If you need me -- if you don't remember that it was Santos, I can show you how we got there.
A. I reference Santos in my --
Q. Okay.
A. -- in my report.
Q. Okay. So if you take a look at this, could you show us where the acetaminophen reference is here?
And did you actually look at the -- did you pull this paper and look at it --
A. Yes, I have.
Q. -- when you did your rebuttal report?
A. Yes, I have.

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Yeah, so this describes the methodology that I used. It doesn't specifically indicate acetaminophen.
Q. But your rebuttal report says acetaminophen?
A. Yes, because I used acetaminophen and applied the methodology in this paper.
Q. If we look through Exhibit 4 and all the supplemental materials, we'll never see a mention of the word "acetaminophen." We'll never see the drug, the compound, correct?
A. As I indicated, I used the methodology in this paper and put acetaminophen into the database and used the methodology that's described in this paper.
Q. You signed your name to a report that says 273 genes are reported to interact with acetaminophen and ASD, correct?
A. In the Comparative Toxicogenomics Database, yes.
Q. Okay. And the backup for that, in that database, doesn't say the word "acetaminophen," correct?

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A. The database does say acetaminophen. If you query acetaminophen, I believe the second hit to come up is autism.
Q. And, Dr. Cabrera, my question is different.
The backup for that 273, when you -- in the database is this paper, right?
A. It's not only this paper.
(Cabrera Exhibit 5 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Well, let's take a look. Can we mark that as Exhibit 5, please?
Dr. Cabrera, you now have in front of you what's been marked as Exhibit 5.
Do you have that in front of you?
A. Yes, I do.
Q. Okay. Does this look like the database that you queried online?
A. It is a printout from the database.
Q. Okay. And the second line is what you were talking about in this rebuttal report, correct?

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A. That is correct.
Q. Okay. And in the database, you see it says 273 genes, and then there's a little plus sign?
A. I do see that, yes.
Q. Okay. Did you click on that when you were in the database?
A. Yes, I did.
Q. Okay. And that's how you got to Santos, right?
A. No. If you click on the references, which is two over, it indicates there are 35 references supporting those 273 genes. And so if you click on those 273, you should see 35 references listed.
MR. MURDICA: Can we mark this as Exhibit 6, please?
(Cabrera Exhibit 6 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Cabrera, you now have in front of you what's been marked as Exhibit 6.
Do you recognize this?
A. Yes, I do.

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Q. Okay. Is this what you would see if you click the link?
A. Yes, it is.
Q. Okay. The first reference is Santos, correct?
A. Yes, it is.
Q. Santos is the reference for 219 of the 273 genes you're saying interact with acetaminophen in ASD, correct?
A. That is correct.
Q. So 219 of the 273, we looked at the article, has absolutely nothing to do with acetaminophen in the words on the page, correct?
A. To be clear, it indicates xenobiotics, and it doesn't list all of the xenobiotics it analyzed in that publication.
Q. Dr. Cabrera, Santos represents 219 of the 273 gene interactions you're relying on in this statement in your rebuttal report, correct?
A. It does.
Q. Okay. And Santos does not contain the word "acetaminophen" anywhere in the paper or the supplemental materials as

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far as you know, correct?
A. As I indicated, it indicates that they've studied 397 gene environment interactions. And the database indicates that it's inferred and, therein, one of those gene interactions would be acetaminophen.
Q. Okay. Was this page of the database peer reviewed, to your knowledge?
A. Not that I'm aware.
Q. And you have no proof, other than it says it's inferred in this database, that Santos actually stands for anything to do with acetaminophen, correct?
A. Well, as I -- as I sit here not in front of the database, and I can't pull up the Santos data to show you, I would simply say there are 397 gene environmental interaction pairs that they looked at in Santos, and they don't list all 397 of them in the report.
Q. Right.
And, Dr. Cabrera, did you look at any of these other on Exhibit 6 here?
A. Yes, I did.
Q. You did? Okay.

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And did you find any that actually had the word "acetaminophen" in them?
A. Yes, I did.
Q. Okay. Do you know which ones? Well, let's -- how about we try the second one?
A. Yes.
Q. Have you looked at the second one, Doan, D-o-a-n?
A. Well, all of them indicate, inferred, except for 3, which is G, and G indicates it's not an inferred. That's a mechanistic interaction.
Q. Okay. So if we look at everything except reference 3, we're not going to find any reference to acetaminophen in the publications, correct?
A. We'd have to look at them individually, but the -- but the inferred versus the mechanistic interactions are -- typically it's based on database analysis of those interactions.
Q. I mean, I have them all. We can look at them all.

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None of them say "acetaminophen" in the data or the supplements.
Do you disagree with that?
A. G says "acetaminophen," and that I've reviewed that study previously, and it says "acetaminophen" specifically in that title and provides dose-responsive evidence of interactions with ADHD and ASD.
Q. G is one of the human studies that we're going to -- well, it's the cord blood study we're going to be looking at that's throughout your report, correct?
A. Yes, it is.
Q. Okay. The others, every other one of these, did you pull them?
A. I did look at them.
Q. Okay. And you never saw the word "acetaminophen" in any of them, correct?
A. Yeah, there -- they -- it's based on genetic interactions. That is, genes that have been associated with ASD that have been associated with exposures.
Q. Right.
But those papers don't actually

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stand for that proposition that the genes have been associated with acetaminophen and ADHD in the words that are on the page, correct?
A. We would have to look at them individually. That being said, the database indicates that there's -- they're inferred interactions based on a gene in a given study or based on a number of genes depending on the study.
(Cabrera Exhibit 7 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Well, let's look at another one just so you feel comfortable that I'm representing it correctly to you. You have in front of you what's been marked as Exhibit 7.
Do you see that, Dr. Cabrera?
A. Yes, I do.
Q. This is what is reference 2 on Exhibit 6, which is the reliance list for your 273 genes, correct?
A. And what reference study is this?

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Q. It's reference 2 on the exhibit in front of you.
A. Oh, I see, yes.
Q. Do you agree?
A. Yes.
Q. Okay. And this is -- you're counting this as six genes that, according to you in your supplemental -- in your rebuttal report, are genes that interact with acetaminophen in ASD, right?
A. To be clear, that's from the database that there's -- it's inferred that these six genes interact with acetaminophen.
Q. You're relying on the database that the database has it right, correct?
A. I am.
Q. Okay. Take the time if you want to look through there. You're not going to find acetaminophen, but when you're comfortable that you can't find it, you let us know.
A. Okay. My reading of this is that the genes that we reported in this genome-wide association study are also genes that have been reported to be changed in

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expression with acetaminophen.
Q. Okay. And it says that in there?
A. It doesn't mention acetaminophen specifically, but in another part of the database, you can look at the specific gene interactions that are reported that you don't -- you didn't present before me.
Q. And it's not -- so you're saying it's not cited in the article, but somehow that article still stands for the proposition about acetaminophen?
A. So the genes that are in this article --
Q. Yeah.
A. -- are genes that are -- have changes in regulations in response to acetaminophen, and the genes that are reported in this article are associated with autism.
Q. Okay. And the information about their interaction with acetaminophen is not coming from that article, correct?
A. It's not, so that's -- the

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expression data shows that there's changes in genes, and those same genes are in this study where there's an increased risk for autism.
Q. And that's a supposition, right? You didn't go and look at every gene in the database, did you?
A. I did not check all 273 genes.
Q. You're relying on --
A. I did look at them all, and I did -- didn't do analysis on them, all of them, but I -- you know, as I -- as I say here, I couldn't -- I don't have the list in front of me.
Q. Okay. Did you look at the methodology of how the database infers that genes are related to something?
A. Yes, just how I described here.
Q. You looked at their stated methodology on their -- in the database?
A. Yes.
Q. There's a page that says it, right?
A. Yes, there is.
Q. And what it essentially does is it combs the literature for any one of

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200 words it -- that in any way correlate, relate, associate, any gene to any compound, exposure or outcome in any way, just in words in the English language, correct?
A. That is the query, but you can also then query further and look for specific interactions. So if you want to look at genes that went up, you can actually look for genes that went up.
If you want to look for genes that went down, you can look for specifically genes that went down.
If you want to look for physical interactions, mechanistic interactions, you can also look at mechanistic interactions.
Each one of those is an option for the database.
Q. This query that resulted in 273, however, was what I described; it was not a more specific inquiry, correct?
A. Yes, it was the general analysis of interactions.
Q. Okay. Now, throughout this rebuttal report that we marked as Exhibit 2,

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I believe, you criticized -- most of it is spent criticizing the analysis of Dr. Chung, correct?
A. That is correct.
Q. And you understand Dr. Chung has offered an opinion here that for ASD and ADHD, the predominant cause in any human being is genetics, correct?
A. That's my understanding.
Q. And you, Dr. Cabrera, disagree with that, right?
A. The principles of teratology indicate that it's genes and environment, that any exposure that can produce an outcome can be modified by the genotype or the background of that exposure.
Q. There are human beings with autism and ADHD that have those conditions 100 percent because of a genetic mutation, correct?
A. They're all -- there are some genes that are what is referred to as necessary and sufficient to cause autism or autism behaviors in people with those mutations, that it's part of the different

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types of genes that interact.
As I mentioned earlier, it's oligogenic, some genes that are necessary and sufficient in themselves to cause autism, and there's also the polygenic and those that can modify risk with interactions between gene-gene interactions and gene-environment interactions.
Q. And, in fact, in your -- in Exhibit 2, your rebuttal report, you criticize Dr. Chung in that you say she relies on -- primarily on the most severe versions of autism and ADHD in her data, correct?
A. To be clear, I was pointing out the exclusion of literature in regards to a clinical diagnosis of autism based on the current guidelines as opposed to some other measures of parameters consistent with autism or consistent with ADHD, that excluding those is one way to strengthen a genetic interaction.
Q. And the implication, is it not, is that you think the more severe versions of autism and ASD are -- autism and ADHD are

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genetic, correct?
A. There -- it's been shown that they're -- they have a stronger genetic interaction or a stronger likelihood of being caused by genetics.
Q. And did you look at Dr. Chung's qualifications prior to criticizing her in your rebuttal report?
A. Yes, I did.
Q. Okay. And you don't have any of the qualifications that she has, correct?
A. I don't have her same qualifications.
Q. Right.
No board certifications in genetics, correct?
A. I'm not boarded in genetics.
Q. Okay. Right.
None of the degrees or accomplishments that she has publicly in genetics are held by Dr. Cabrera, correct?
A. I don't have the same accolades as her, if you will.
Q. Okay. And you do know that Dr. Chung's opinions that she's rendered here

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are consistent with all of the medical organizations that have looked at this, correct?
A. I disagree --
MR. TRACEY: Objection to form.
THE WITNESS: -- inasmuch as Dr. -- Dr. Chung's opinions aren't consistent with Dr. Chung inasmuch as her own presentations and her work outside of defense work.
QUESTIONS BY MR. MURDICA:
Q. I know you -- I know you -- well, I'm not going to argue with you about that.
Have you seen what the medical organizations have said about acetaminophen and whether or not they relate to autism and ADHD?
MR. TRACEY: Objection. Form.
THE WITNESS: Collectively, my understanding is they're still under review by the FDA.
Outside of that, I'm -- you know, unless you're speaking to a specific medical organization, I can't

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comment.
QUESTIONS BY MR. MURDICA:
Q. Sure.
How about -- well, let's talk about in your field.
Did you see what OTIS said about this?
A. I have, yes.
Q. They disagree with you, correct?
A. Apparently.
Q. Not apparently, they do, correct? You've seen it?
A. I've seen it.
Q. Yeah.
And it's not just -- OTIS is more than one person, correct?
A. It's a group.
Q. It's a group, and the whole group disagrees with you, correct?
A. I don't know that the whole group does. I didn't --
Q. Well, as a group --
A. I can't -- I can't say that.
Q. As a group, they disagree with

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you, correct?
A. OTIS did put out a position piece, and I don't know that it was OTIS in its entirety, but OTIS did put out a position piece to that effect.
Q. And what does OTIS stand for?
A. It's the --
Q. Is the "T" teratology?
A. Yes, Obstetrics, Teratology Information Society {sic}, I believe.
Q. Okay. MotherToBaby?
A. It's part of it.
Q. Okay. And FDA disagrees with you, correct?
A. My understanding is FDA is still reviewing the information.
Q. Well, have you looked at what they've said?
A. Recently as -- 2015 was the recent opinions that they offered, but that was -- there's been quite a bit of data since then.
Q. Okay. Dr. Cabrera, didn't you look at documents produced by the FDA in the litigation?

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A. Yes, I have.
Q. Aren't those more recent than 2015?
A. Oh, yes.
Q. They're as recent as 2022, correct?
A. Yes.
Q. And the conclusion that they have and the reason why nothing has changed with respect to acetaminophen is because they disagree with you, correct?
MR. TRACEY: Object to form. This is not a re -- {inaudible} -- deposition.
THE WITNESS: Yeah. I don't agree with that. I think it's still under review at the FDA. That's my understanding.
QUESTIONS BY MR. MURDICA:
Q. Okay. They have not come to the conclusions, publicly or privately, as far as we know, based on the documents you reviewed that you have, correct?
A. I have not seen --
MR. TRACEY: Object -- object

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to the form.
THE WITNESS: Yeah, I have not seen that -- a public opinion that has changed since the 2015 statement by the FDA.
QUESTIONS BY MR. MURDICA:
Q. You have not seen a public opinion or documents that are consistent with your opinion here, correct, from FDA?
A. I have not seen that from the FDA publicly or in their other documents, other than the fact it's still under review.
Q. And did you see what FDA said about this as recently as last month?
A. There was a statement last month. I'm not sure I've seen that statement.
Q. Okay. I'll show you in a minute, in the interest of moving this along.
I asked you about OTIS and FDA.
Did you look at what ACOG has said?
A. I'm familiar with the ACOG rebuttal statement.
Q. Right.

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Okay. So you know they disagree with your position here as well, right?
A. Consistent with the rebuttal statement, I'm familiar with that.
Q. Okay. And same with the Society for Maternal-Fetal Medicine, right?
A. I haven't seen the statement for Society for Maternal and Fetal Medicine.
Q. Okay. Well, let me ask it this way. Have you seen any medical organization that agrees with you -- that agrees with your opinions here, Dr. Cabrera, as it relates to acetaminophen and autism and ADHD?
A. I have not seen a statement from a medical organization, no --
Q. Are you --
A. -- in that regard.
Q. -- concerned by helping the plaintiffs here you're contributing to a public health crisis?
A. To be clear --
MR. TRACEY: Objection. Form.
THE WITNESS: To be clear, I'm not -- there is -- there is a public

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health concern for safety, and that's the lack of warning on the label.
QUESTIONS BY MR. MURDICA:
Q. You're not concerned that by being a part of a lawyer movement to scare pregnant women about the use of acetaminophen that you can harm them --
MR. TRACEY: Robert, Robert, don't answer that question. It's nonsensical. It's argumentative, and it's outrageous for a scientific deposition.
If you want to ask a question grounded in science, that's relevant to general causation, do it. If you want to make speeches, go out on the street.
MR. MURDICA: Okay. Well, my response to that is that he's offering labeling opinions in his -- in his report, Sean. I could cite the pages to you, but there's several pages on it, so...
He also, Sean, just testified that there is a public health concern,

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so I'll come back to that in a minute.
MR. TRACEY: It was -- it was the way you asked your question loaded with all sorts of arguments that were probably created within the confines of your firm or Johnson & Johnson.
Ground your questions in something factual.
MR. MURDICA: Sure.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, earlier we talked about the thimerosal literature and the events surrounding thimerosal and the concern for autism.
Do you recall that?
A. Yes, I do.
Q. There was a public health issue with thimerosal that caused children to not be vaccinated because of a scare of autism in the vaccine, correct?
A. I'm familiar with that idea. I don't know about that endpoint.
Q. Okay. And that ended up being not true. I think we talked about that earlier, or at least the data has not proven

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it, correct?
A. Fair enough.
Q. And you know, as a human being in society, that that has had long-term consequences where some people don't want to vaccinate their children, correct?
A. I'm aware that that has created some vaccine hesitancy in the population.
Q. So my question is, as a researcher at an institution like Baylor, are you not concerned that you are causing thimerosal part 2 by rendering an opinion like you are here?
A. So there are potential public health impacts in that regard. I am aware of that.
MR. MURDICA: Okay. Let's mark this as Exhibit 8.
(Cabrera Exhibit 8 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, you have in front of you Exhibit 8, and I just asked you about whether you had seen a recent FDA statement on this topic. You seemed unfamiliar with

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it.
Have you seen this before?
A. I can't say that I have.
MR. WATTS: What's the date on it, Jim?
MR. MURDICA: It's July 10, 2023.
MR. WATTS: Thanks.
QUESTIONS BY MR. MURDICA:
Q. Doctor, if you turn to -- unfortunately, the pages aren't numbered. I will -- let me help.
And feel free, you can read anything you want. My question is going to be about this paragraph.
A. If we could take a break so I can actually read this and do a bio break.
MR. MURDICA: Totally fine. Yeah. Yeah.
MS. KING: Can we go off the record?
MR. MURDICA: Yeah. We'll go off the record.
VIDEOGRAPHER: Off the record, 11:25.

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(Off the record at 11:25 a.m.)
VIDEOGRAPHER: The time is 11:43, back on the record, beginning of Media 3.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, are you ready to proceed?
A. Yes.
Q. Okay. I had asked you a question before we took a break. I can ask it again, but in the meantime, did you have a chance to review what's been marked as Exhibit 8?
A. Yes, I did.
Q. Okay. And my question for you was about -- you see it's dated July 10, 2023?
A. Yes, I do.
Q. Okay. And in it, it is a -- a reporter is attributing to FDA Press Officer Charlie Kohler an e-mail where FDA has said, "'While the agency continues to monitor the issue, it closed the formal tracking process in 2020,' said Kohler, because extensive reviews failed to turn up solid evidence of

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the link between the drug and neurodevelopment issues."
Do you see that?
A. One second here.
Q. Do you want me to give you the page?
It's before that. Oh, no --
A. This one here?
Q. Yep.
A. Okay.
Q. You have it flagged, I think.
A. Yeah. Okay. Yes.
Q. Okay. You saw that when you reviewed it --
A. Yes, I did.
Q. -- during the break, right?
Did you know before today that as recently as July 10th of 2023, the FDA made such a statement?
A. I see that this press officer has made this in this article. I hadn't seen this article previously.
Q. Okay.
A. So I was unaware of both this article and that statement.

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Q. Okay. And the statement here by an FDA press officer less than a month ago disagrees with the opinions you've rendered in this litigation, correct?
A. Well, what it indicates is, as you -- as you've read, according to this press officer, that the formal tracking processes in 2020 closed, and that they failed to turn up solid evidence of a link between the drug and neurodevelopmental issues. And I do disagree with that statement.
Q. Right.
Because you believe you turned up a solid evidence of a link between acetaminophen and neurodevelopmental issues, correct?
A. Because there is solid evidence of that.
Q. As of when -- Dr. Cabrera, as of what date, based on your review, is there solid evidence of a link between acetaminophen and neurodevelopmental issues?
A. I would say there's been growing evidence since at least 2015.

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Q. Okay. Since FDA first said -- you referred to earlier in response to a question of mine that you were aware of an FDA statement in 2015, correct?
A. Yes.
Q. And we're both talking about the same thing. It's what you can find on FDA's website that says while there have been these studies, there's no reason to change current guidance for how acetaminophen is used, correct?
A. That is correct.
Q. Okay. And you're saying right about then is when there was a solid link between acetaminophen and neurodevelopmental issues?
A. I'm saying there's been growing evidence since then in support of a causative interaction between acetaminophen and neurodevelopmental issues.
Q. Right.
And at what point -- is it 2015 -- what was available as of 2015 would have led you to the conclusion that it causes ASD and ADHD?

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A. I would say the authoritative reference in Maternal and Fetal Medicine changed its warning about acetaminophen in 2015. So that would be consistent with the growing evidence, and that's the same warning that it still carries to this day.
Q. Well, I'm asking about your opinions, Dr. Cabrera.
Based on your review, because you looked at -- we're going to go into all the stuff that you looked at over lunch, but you looked at articles from the 1980s, right, the 1990s, 2000s? You looked at -- you handed me today something from two days ago, right?
A. (Witness nods head.)
Q. At what point in time, according to Dr. Cabrera, was there enough evidence to believe that there was a causal relationship between acetaminophen and ADHD and ASD?
A. I would have difficulty retrospectively telling you as someone that wasn't following it longitudinally to tell you when the exact time that these things

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should have changed. But I can tell you that the reference textbook, which is considered essential for education in the health sciences, indicates that that label changed -- or their labeling of acetaminophen changed in 2015.
Q. And which reference textbook is that?
A. That's Briggs.
Q. Briggs.
And was that with respect to ADHD and ASD or just ADHD?
A. Initially, it is with ADHD, but it also includes other neurodevelopmental disorders.
Q. And when was that?
A. That started in 2015.
Q. Okay. So in 2015, it included autism in Briggs?
A. It didn't include autism initially. It was ADHD initially.
Q. And that is -- Briggs is a textbook that you used?
A. It is a textbook that I -- that I reference.

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Q. Okay. And do you know what Briggs did to come to that conclusion?
A. They conducted an analysis of the literature.
Q. And they said that it's causal?
A. They made a pregnancy summary specific to that in 2015 and highlighted it as a fetal risk summary and then described the literature in that regard. And it changed from being compatible with pregnancy to human data suggests low risk and fetal risk and then described the summary of that risk.
Q. Okay. And is Briggs something that you use to make your causation determination, or did you do that independently?
A. I looked because I -- as I mentioned previously, I do have a specialist in maternal-fetal medicine, and she said to look at it in the book and see what they said. Like, that would be what would be the current guidance for actual medical professionals. And so that's what I looked. This is what they get educated with.

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Q. Right.
Medical professionals which you are not, correct?
A. I am not a medical professional.
Q. And in your work in teratology, had you ever looked at Briggs before?
A. I've looked up things in Briggs before, yes.
Q. Okay. Is that a reference textbook you use in teratology?
A. For looking up compounds, you can, absolutely. It's online, so it's easy to access.
Q. Yeah.
I'm saying in your work, is Briggs a standard reference for you as a teratologist and has been?
A. Yes, specific for human exposures because they tend to focus more on what's the clinical recommendations in regards to patients.
Q. Okay. So Dr. Cabrera, for his opinions here, is relying on Briggs summary of articles in 2015, correct?

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A. I included it as part of the data, their review as well.
Q. Right.
And that is an underlying part of your causation opinion, to rely on their review of articles from 2015, correct?
A. I did review their work as well as part of the literature that I looked at.
Q. Okay. I just want to be clear.
As part of your causation opinion here, you are relying on Briggs' own review of the literature in 2015, correct?
A. I'm simply referencing them as authoritative texts. Authoritative texts are not part of causation. So that's not part of the causation analysis, but it was part of the analysis I conducted --
Q. Okay.
A. -- in regards to background.
Q. Right.
Because you can look at the articles yourself. You don't need to rely on Briggs' interpretation to come up with your interpretation, correct?
A. That is correct.

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Q. And nothing in Briggs says that, 2015 or now, that acetaminophen causes ADHD, correct?
A. The pregnancy summary indicates, "Although the risk is very low, use of the drug for several weeks or longer has been associated with cryptorchidism, decreased IQ, ADHD and other problems in neurodevelopment." And "other problems" are largely referenced. Some of them overlap with autism and including intellectual disability.
Q. Okay. And so back to my question.
Whether it be in 2015 or today, Briggs does not say that acetaminophen causes ADHD or autism, correct?
A. It says that it has been associated with and that short-term use suggests low risk, long-term use suggests risk of, as I just mentioned, cryptorchidism, decreased IQ, ADHD and other problems in neurodevelopment.
Q. Okay. Is there a difference between association and causation,

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Dr. Cabrera?
A. There is.
Q. Okay. And association is not causation, correct?
A. That is correct.
Q. Your opinion here is that acetaminophen causes ADHD, correct?
A. That is correct.
Q. Your opinion here is that acetaminophen causes autism, correct?
A. That is correct.
Q. Briggs, whether it be in 2015 or now, does not say that acetaminophen causes ADHD or autism, correct?
A. It's not a causation analysis.
Q. Okay. Thank you.
Now, let's talk about some other things that you considered and -- because I want to know if they're a part of your causation opinion or just things that you considered.
I saw on your reliance list that you looked at documents from the manufacturer of Tylenol.
Is that right?

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A. Yes.
Q. Okay. And that was your idea, right?
A. I asked for documents in regards to preclinical studies.
Q. Okay. And how do you know that you got everything that was available?
A. I don't know that for a fact.
Q. Okay. So did you ask anyone how many pages or how many documents were produced in litigation with respect to Tylenol?
A. I haven't asked that.
Q. Okay. Do you know how many pages you did get?
A. I -- all the pages I did get are in my work cited or my reliance list. Outside of that, I -- I probably haven't seen it, if it's not in my reliance.
Q. Okay. So before I ask you any questions about them, are these things like Briggs that you considered but they aren't part of your causation opinion, or are they part of your causation opinion?
A. Things that I considered.

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They're not part of a causation analysis.
Q. Okay. And in your normal work, you're looking at science, not at company e-mails or anything like that, correct?
A. That is correct.
Q. Company e-mails and deposition transcripts don't really elucidate the data that you're considering for causation, correct?
A. That's generally outside the scope of -- other than e-mails within Baylor, as an institution, I wouldn't normally look at institutions from -- e-mails from other institutions.
Q. Okay.
A. Or other companies.
Q. All right. Before we break for lunch, I just want to go back to some of the questions I had for you earlier regarding pregnancy -- we talked about a pregnancy registry.
Do you remember that?
A. Yes.
Q. I just want to talk to you briefly about hierarchy of evidence.

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Here, when you're looking at acetaminophen and whether it can cause ADHD or autism, is -- do you agree with me that we don't have the quality of data that would be the equivalent of the NAAED we were talking about earlier? In other words, a pregnancy registry double-blinded in humans?
A. It's two questions. Which one do you want me to answer?
Q. Okay. Here --
MR. TRACEY: Objection. Compound.
MR. MURDICA: You cheated. He gave you that one.
MR. WATTS: Objection. The witness is leading Mr. Tracey.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, with respect to the data available for acetaminophen exposure in utero, does a pregnancy -- a double-blinded pregnancy registry exist?
A. Yes.
Oh, no, no. For acetaminophen, no.
Q. Okay. And so we don't have

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prospective, double-blinded human pregnancy data with respect to acetaminophen, correct?
A. Not that I'm aware.
Q. Okay. And in the hierarchy of evidence, that would be really high if we had it, correct?
A. In the hierarchy of evidence, I would -- I would put that just below meta-analysis.
Q. Okay. And below that, what do we have?
A. Well, any prospective studies and then retrospective studies.
Q. Okay. And there's very -- there's differences in prospective studies, right? Some are a higher quality than others, right?
A. There can be, yes.
Q. Okay. And whether they're controlled or not, correct, makes a difference?
A. Yes.
Q. Do you agree?
Clinical trials, for example, would be high up on the scale of evidence,

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right?
A. Well, clinical trials would normally fall in double-blind, you know, studies. So those would be high.
Q. And generally, in the United States, as an ethical matter, we don't intentionally test drugs on pregnant people, correct?
A. Yeah. To be clear, I think that's fairly global, that we don't include pregnant women in drug testing.
MR. MURDICA: Okay. All right. I'll get into this stuff after lunch so that the food doesn't get cold. All right. Thanks. I don't want anybody getting mad.
VIDEOGRAPHER: Off the record?
MR. MURDICA: Yeah. We'll go off the record.
MR. TRACEY: How long is the lunch break?
VIDEOGRAPHER: Off the record, 11:59.
(Off the record at 11:59 a.m.)
VIDEOGRAPHER: The time is

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12:48 p.m., back on the record, beginning of Media 4.
QUESTIONS BY MR. MURDICA:
Q. Welcome back from lunch, Dr. Cabrera.
Are you ready to proceed?
A. Yes, I am.
Q. Okay. All right. We're going to get back into it with some easy ones.
I think you acknowledged earlier that you're being paid for your time here by plaintiffs' lawyers, correct?
A. Yes, I am.
Q. And what's your hourly rate?
A. 500.
Q. Okay. And how much have you charged them so far in this litigation, ballpark?
A. I think I had about 200 hours or so. Maybe just over 200 hours.
Q. So over $100,000, thereabouts?
A. Approximately, yes.
Q. Okay. And how does that compare to your -- whatever you get paid by Baylor or your lab?

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A. It's -- relatively speaking, it's about --
MR. TRACEY: Hold on, Robert. You don't have to answer personal financial information about how much money you make. That's not relevant.
MR. MURDICA: It does go to bias, if it's 100 percent of what he makes, Sean.
MR. TRACEY: Are you going to let me ask all your witnesses how much their salary is at their places of employment?
MR. MURDICA: I'm not asking his salary. I didn't ask his salary. I just asked how it compared to what he's being paid. Could be significant, could be insignificant. I didn't -- I didn't tell him how to answer it.
MR. TRACEY: Well, I know, but you left -- that question is open-ended. I don't know how else any, you know, nonnormal lawyer would answer that.

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MR. MURDICA: If I didn't ask it open-ended, you'd object.
MR. TRACEY: Well, try me and see.
MR. WATTS: Are we going to ask about money at every deposition, or do you want to not do it? I don't care. You decide.
MR. MURDICA: I'll pass.
QUESTIONS BY MR. MURDICA:
Q. Okay. One of the principles of teratology is to consider all evidence when you're trying to make a causation determination, correct?
A. The totality of evidence, yes.
Q. Okay. Do you feel that you followed that here?
A. Yes.
Q. Okay. So there's nothing you intentionally didn't consider, correct?
A. Not intentionally.
Q. Okay. In your -- you have access to your lab that you were talking about earlier, right?
A. That's correct.

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Q. And in your regular work, you -- your primary work, you conduct rodent tests, right?
A. We do three things in my laboratory that is both genetics, and that includes human and animal genetics.
And so we have a human genetic side, and we make mouse models of human disease, we refer to that as the mouse side. And then we also do tissue culture and produce cellular models of diseases. And that's -- by and large, it's turned into stem cell cultures. So we make -- induce pluripotent stem cells, and we do embryo cultures or neural cultures.
Q. So you work with cells?
A. Yes.
Q. And you work with rodents, and you do process or -- do you do genetic testing there, or do you send it out?
A. For clinical testing, that gets sent to Baylor Genetics. For research purposes, we do -- we do research.
Q. Okay. And when you were asked to look into acetaminophen here, did you

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conduct any tests in your lab?
A. I have not.
Q. Okay. You didn't conduct any cellular tests?
A. To be clear, that would be a conflict of interest if I was doing tests with acetaminophen while I was being paid. I would have to file that as a conflict of interest with Baylor.
Q. Okay. Can you explain that to me? I don't really understand how that's a conflict of interest.
A. Because I'm being paid, in order to do research at Baylor with the resources that I -- that I have, I would have to file that with Baylor; that I would be using my resources to do research --
Q. I see.
You can't use your lab to do outside research; is that what you're saying?
A. To do my personal research.
Q. Okay. You could have used your expertise to borrow a lab or rent a lab and done acetaminophen research, correct?
A. That would be a possibility.

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Q. Okay. And you didn't do that, right?
A. I have not.
Q. Okay.
A. Well, not in this case, no.
Q. Do you anticipate doing that in this case, sitting here today?
A. That is not something I planned on doing.
Q. Okay. Have you looked at the records of any person in relation to this litigation, any human being?
A. Case-specific?
Q. Yes.
A. I have not looked at any case-specific.
Q. Okay. By the way, earlier you said that somebody told you to look at Briggs, and we talked about that for a while.
A. (Witness nods head.)
Q. Who is the person who told you to look at Briggs?
A. One of the people in our group. Her name's Jackie Parchem.
Q. Okay. And what's her

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specialty?
A. She's maternal-fetal health. She's an -- she's an obstetrician, gynecologist.
Q. And can you -- I didn't hear the last name. Jackie?
A. Parchem.
Q. Parchem?
A. Yeah.
Q. Okay. And I believe you said you recognized Briggs as an authoritative textbook?
A. Yes, I do.
Q. Okay. What other textbooks do you recognize as authoritative?
A. So what I was trained in for human development is human embryology is -- usually they are -- I think that's some -- Moore's is the textbook --
Q. Moore's.
A. -- we use for human embryology.
Q. Okay.
A. And it's the same -- it's a medical school class. It's the same book that they teach both graduate and medical

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students in that class and under the -- and using the same book.

So for human embryology, that was the book we used for human embryology.

Q. Any others?

A. Yeah, there were -- there were others.

Q. Okay. Well, I know you testified earlier that you looked to Briggs as an authority, and you use it in your regular teratology practice. So now we -- now we have one more.

Are there any others that are, you know, your regular teratology books you look towards?

A. I reference Moore, I believe, in my report as well, as part of my reliance. I -- I'd have to look at my reliance list to see what other texts that I did reference in there, but those are -- those are two that I refer to regularly.

Q. Okay. And just going back to something earlier, Mr. Tracey objected when I asked about your meetings with other experts. So I'm not going to ask about -- anything about those.

But did you have any role in responding to our deposition notice and the answers to those?

A. We went through them.

Q. Okay. Do you recall answering that you had not interacted with any other experts in this litigation?

A. Inasmuch as we went through the -- I -- it was only with the lawyers, and so I think they would be familiar with that, if that was --

Q. Yeah. I'm not going to ask about anything that happened, but my understanding, unless I misread it, is that your answer was that you hadn't interacted with any of the other experts.

But that -- we know now that's not the case, right?

A. With the -- with the lawyers and on call, we did have -- I have -- I have spoken with some other --

MR. TRACEY: Robert, don't say anything else.

THE WITNESS: Okay.

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MR. TRACEY: That's all privileged.

MR. MURDICA: I'm not going to ask anything else.

THE WITNESS: Okay.

MR. MURDICA: I was just asking in the context of the discovery responses.

QUESTIONS BY MR. MURDICA:

Q. Okay. And one last follow-up on something we talked about earlier.

You remember I showed you I believe it was Exhibit 4, the Beyer study, and I asked you about CIC, and you said it was in the supplemental tables online.

A. Oh, I told you this was the methodology that we used -- are you talking about Santos?

Q. No.

A. It was 4.

Q. Sorry.

A. Oh.

Q. 3 maybe.

MR. CHARCHALIS: Beyer is 3.

MR. MURDICA: 3, okay.

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THE WITNESS: Okay. Yes.

QUESTIONS BY MR. MURDICA:

Q. Remember I -- this was from your rebuttal report. We were talking about I believe it was capicua and CIC in your report?

A. Yes.

Q. And I said where is it in the study, and you said it's in the supplemental tables?

A. I said I'd need to check the supplemental tables, yes.

Q. Okay. So we had checked before --

A. Yes.

Q. -- and we checked again.

We don't see it. Is there -- is there anything else -- other than CIC or capicua, is there anything else that you would look to, any names somehow we're missing?

A. I -- I'd have to look at the database --

Q. Okay. But you --

A. -- in front of me and --

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Q. I'm not asking you to agree. I'm just asking you if there's any other name you would refer to that gene by or --
A. Oh, the name of the gene?
Q. Yeah.
A. Those are both the gene names that we -- we've used. It may have had a name before that, but I would -- I'd have to look that up in the database.
That should be available in GeneCards if you were looking for aliases.
Q. Okay. So sitting here today, you're not telling us that it's definitely in the tables. You agree it's not in the article, but you're also not telling us that it's in the tables; you just don't know?
A. I would have to look specifically at the -- at the database and mine in the database to show you exactly where everything is, but the interactions are there.
I can -- I looked at them. I've seen them. I think you're just -- you're not in the right place in the database.

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Q. Okay. But you believe you either saw CIC or capicua in the database?
A. It's in the database.
Q. Okay. And not in that article, Exhibit 3, itself?
A. I'm looking at -- I -- as we just looked at the article, I did not see capicua in that article, but it is in the database.
Q. Okay. All right. Let's talk about one more principle of teratology.
You know that the Teratology Society about 15 years ago published guidelines for considering causation in litigation, right?
A. I mean, if you're asking me if there's a publication about that, I'm aware that there's a publication about it.
Q. Right.
You've seen it before. It's been shown to you before in litigation, right?
A. I have seen it before.
Q. Okay. Did you look at it before rendering your opinions here?

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A. I'm -- yes, I am familiar with it.
Q. Okay. And any causation opinion and any data you used to reach the opinion, one of the principles is it needs to be outcome-specific, correct?
A. Specificity is part of Bradford Hill in that regard.
Q. Yeah.
And I'm asking you about your Teratology Society and the principles. When you render an opinion as a member of that society, it's supposed to be outcome-specific, right?
A. Just to clarify, that position paper, which, you know, if we're going to talk about it, we should -- we should have it in front of us, but I am familiar with it, in as much as the correspondence on that's Tony Scialli, and that position is not a position of the Teratology Society as a whole. I believe that was part of the public affairs committee.
Q. Okay. What it means -- well, do you -- did you disagree that you should be

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looking at evidence that refers to the outcome you are opining about?
A. You should absolutely look at -- look at the outcome.
Q. Right.
And here, the outcome is ASD or ADHD. You have two outcomes you're looking at, correct?
A. I did look at those two outcomes, yes.
Q. Those are the two outcomes that you were asked to look at, correct?
A. I was asked to look at ASD, ADHD and -- as specific outcomes, yes.
Q. Okay. And so according to that principle, the evidence on which you base your causation opinion should be ASD and ADHD data, correct?
A. Well, I'm not going to say that those principles are the -- are definitive or even authoritative in that regard, but if you want to talk about those -- what the publication says, then we should have it in front of us specifically.
Q. Well, you don't know? It's --

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you're a member of the Teratology Society.
A. I wouldn't take it upon myself to memorize anything Tony Scialli said.
Q. Okay. So I'm just asking you then, do you think that that's what you should consider in rendering a causation opinion?
A. You should consider the totality of data. We already talked about that.
Q. And the totality of data specific to the outcome, correct?
A. We should -- we should consider those outcomes and also intermediates of those and then parallel outcomes with those.
Q. Okay. Well, you testified in a litigation attributing mental retardation in a patient to trichloroethylene exposure, correct?
A. I'd have to see the particular case you're referring to.
Q. Okay. You don't remember that?
A. I'm -- I would have to see the particular case you're referring to.
Q. How many cases have you

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testified in for plaintiffs?
A. I would have to see the particular case --
Q. Too many to remember, right?
A. I have a list of them.
Q. Where is it? You didn't provide it to us. Where's the list?
A. I was told that the information that I was to provide was within the last few years.
Q. Okay.
A. And that's what I did provide.
Q. Do you have -- do you have a list of all of your testimony you've ever done?
A. Of course.
Q. Okay. And where is that?
A. On my computer.
Q. Okay. Okay. So you don't remember attributing mental retardation to TCE exposure?
A. I'm --
MR. TRACEY: Objection. Form.
THE WITNESS: No. If it's -- if you're referring to a particular

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case that is sealed, I'm not at liberty to discuss.
QUESTIONS BY MR. MURDICA:
Q. It's not sealed.
A. So...
Q. Do you remember a plaintiff Trujillo, Trujillo?
A. I'm familiar with Trujillo.
Q. Okay. Do you remember now what you were alleging the outcome was?
A. I mean, if you want to provide case-specific stuff, we can review it.
Q. Well, what I'm asking you is, mental retardation is a different outcome than autism or ADHD, correct?
A. It is.
Q. Okay. So are you going to rely on the outcome of mental retardation in rendering a causation opinion on autism or ASD?
A. As a different outcome, unless they have overlapping pathology, I would not include it in part of my analysis.
Q. Okay. How about learning disabilities?

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A. So inasmuch as there are some cases with ADHD and ASD that also include learning disabilities, they would be part of an analysis.
Q. But not all -- I mean, we talked earlier, right? Someone autistic can be a savant and they don't have a learning disability, correct?
A. That is a possibility.
Q. So you're going to use, and you did use, outcomes that were not the target outcome as reliance for your causation opinion?
A. If there's overlap in the presentation as part of what's understood about -- particularly with autism itself or animal models of autism is not every case of autism is the same, and some of them have overlap with other pathologies.
And so if those other pathologies included -- were included, then I would -- then I would often include them as part of the analysis.
Q. Is it fair to say that if an outcome in a study was a symptom of autism in

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some patients or some animals, you included that in your analysis?
A. I tried to include the totality of data so that I would be fair in that regard.
Q. In your mind, in Dr. Cabrera's mind, is it -- is it reliable to use symptomatic outcomes rather than the target outcome of ASD or ADHD?
A. It could be informative if it -- if it is occurring with other outcomes that are core behaviors of ADHD or ASD.
If it -- if it's occurring as an endpoint specifically and without overlap of ADHD or ASD, then I would not consider that.
Q. Right.
But in Dr. Cabrera's opinion, any study where the outcome was learning disability counts towards autism, correct?
A. Is not correct.
Q. Why not?
A. Because there are some impacts, and it's even referenced in the -- in the AOP where they indicate that some indications of

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learning disability can be core symptoms of autism or of ADHD.
Q. Right.
And that's why you think that AOP speaks to autism, correct?
A. Well, that's -- not just the AOP, but those are part of the OECD guidelines for testing, that some learning and behavioral effects overlap with autism and ADHD core behaviors.
Q. Okay. And according to Dr. Cabrera, that AOP also speaks directly to autism and that -- the pathway, correct?
A. Yes, because the -- some of the learning and developmental endpoints do overlap with autism, and that's even in the OECD guidelines. Not just the AOP, the OECD guidelines.
Q. Okay. And according to Dr. Cabrera, any neurodevelopmental toxicity also is an outcome that you're looking at to attribute causation for ASD and ADHD, correct?
A. I did include in my analysis any neurotoxicity.

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Q. Right.
But not -- all neurotoxicity does not equate to ASD or ADHD, correct?
A. That's correct. The -- particularly for ASD or ADHD, it would be developmental neurotoxicity that would be more specific for those outcomes, but I did consider neurotoxicity generally as well.
Q. And even if you, Dr. Cabrera, considered only developmental neurotoxicity, that's still a larger pool than ASD and ADHD, correct?
A. There are other endpoints with developmental neurotoxicity such as neural tube defects would be evidence of developmental neurotoxicity that's not ADHD or ASD.
Q. Right.
I think we agreed earlier, neural tube defects are something totally and profoundly different than ASD or ADHD, correct?
A. Well, I don't know about totally different because inasmuch as there appears to be some overlap in the molecular

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pathways, but certainly the -- one is a phenotypic presentation, and one is a diagnostic determination based on clinical diagnostics.
Q. The appearance and the outcome are profoundly different, correct?
A. I agree with that.
Q. Okay. Before the break, we were talking about different levels of evidence that are available, and we were talking about evidence that could be available in humans.
I'm going to ask you -- you focused a lot in your report on animals, right?
A. That's correct.
Q. And you work with animals?
A. I work with people, too, but, yes.
Q. And the animals you work with are -- do you work with rats or just mice?
A. Mice.
Q. The outcomes that you looked at in mice is any developmental toxicity, correct?

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A. I look for developmental toxicity generally, yes.
Q. You included in your review articles that really had anything to do with toxicity in a -- in a mouse embryo, right?
A. So my approach as a teratologist was to look at what Wilson referred to as the four manifestations of deviant development, and those include congenital malformations in addition to functional deficit.
And it may also include death as a potential outcome, which would be the most severe form of that -- of toxicity.
Q. For ASD and ADHD in particular, what outcomes were you looking for in the mouse model?
A. Well, part of looking for these outcomes is understanding the study designs and what information is available in there.
As an example, you have to examine also maternal toxicity. So you have to consider maternal toxicity, even though your -- your question may be, What's the outcome in the offspring, ADHD or ASD, you

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also have to consider maternal toxicity as one of those factors.
So there are -- there are different levels of toxicity because the maternal system is providing the environment, so you have to consider other types of toxicity when you're looking at a particular outcome.
Q. What specifically are you looking for in the mouse to look for autism?
A. So typically we do neurobehavioral testing in the mouse to look for what's referred to as core autistic behaviors.
Q. And in the mouse, since they can't talk to us, you can't actually diagnosis a mouse with autism, correct?
A. They do vocalize, but it's supersonic, so we can't hear them, but we do not use that as part of our diagnosis like you would with a human patient.
Q. And it's the same thing with ADHD, right?
A. So we do neurobehavioral testing on them, and we look for behaviors

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that are consistent -- what's referred to as consistent with ADHD in the animal model.
Q. You look -- right.
You have -- you have guidelines that you believe are behaviors consistent with those, but you can't diagnose a mouse with ADHD or autism, correct?
A. Right. So clinical diagnosis of ADHD or autism requires a clinical diagnosis, and we don't do that type of assessment on the animals. We do neurobehavioral, behavioral testing on them.
Q. Right.
And those are different techniques developed over time that researchers like yourself believe are consistent with neurodevelopmental behaviors, right?
A. I'd say they're generally accepted that these behaviors parallel what we see in the human with similar exposures.
Q. Well, in fairness, humans aren't burying marbles in tanks, correct?
A. They could, but it -- as a normal behavior, burying is perhaps something

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that people and animals may have shared in the past, but not something that we commonly engage in anymore.
Q. You're not looking at human beings who are repetitively -- repetitively grooming or nest-seeking or burying marbles, correct?
A. So we do look at repetitive behaviors in humans. That's part of a clinical diagnosis. So that is part of it, actually.
But in regards to specific behaviors of nest-seeking or marble burying, that's not part of the human clinical diagnosis.
Q. Right.
And, by the way, is nest-seeking in the rodent model a measure for ASD or ADHD?
A. In their recognition of things -- so, like, socialization is part of the ASD or core behaviors. And so disruption in what is partially thought as the olfactory system is -- can be related to that, in that the mouse, unlike the human, which is largely

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visual, the mouse uses smells in order to recognize where it belongs and new people -- or new mice, in this case. As we might recognize somebody visually, they recognize it as smell.

So it's part of an assessment for their social behavior, which would be an important core behavior for the -- for the mouse.

Q. That answer was about nest-seeking?

A. Yes, in order for them to --

Q. So according to Dr. Cabrera, nest-seeking is a relevant behavior in the mouse model for autism and ADHD, right?

A. Well, it assesses a behavior in the mouse that's part of social -- a social behavior. So you're testing a social behavior of the mouse.

Q. So if you have a litter of mice that are more nest -- are nest-seeking more than normal, you would say that's an autistic or ADHD signalling behavior or something like that?

A. So you could go either way. So

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if they spent too much time there, this could be associated with anxiety. If they didn't spend any time there, then this could be a problem with their social behavior. So you have to interpret the data as it comes.

Q. And when you first started doing these experiments on mice, did these behavioral beliefs and tests in mice exist?

A. They've evolved over time.

Q. And do you agree that those behavioral observations are really theories because you can't diagnose and talk to the mice?

A. Well, just to clarify, a theory is a very strong word in science, and I would say that there -- our understanding of those behaviors, that they are part of the social behaviors in the animals. And I don't think that's theoretical. I think that's part of just the reality that they -- that they exist in.

Our interpretation of those is certainly open as far as what that means and how we interpret their behaviors.

Q. I guess that -- let me ask a

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better question, because that was a good point.

Our hypothesis, your hypothesis, is that those behaviors translate in some way to neurodevelopmental outcomes -- neurodevelopmental behaviors in human beings, right?

A. So what we do in -- what I've done for the majority of my career is to make animal models of human disease. And part of making those models of human disease is to see if the animal behaviors any way parallel what we would find in human behaviors, and we do find some parallels in that regard.

Q. Right.

But the behaviors that the animals exhibit are not identical behaviors that are -- that human beings exhibit, correct?

A. Neither -- the diagnosis criteria is not the same as would be used clinically for a clinical diagnosis in humans. It does -- it is different with the animals.

Q. And you agree that the animal

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model, in all aspects, not just neurodevelopment, does not translate directly to humans in many cases, right?

A. There are -- there can be differences, both by differences in species. Thalidomide is the classic example inasmuch as it had a profound effect in humans, but it was initially missed in animals. It was only after they retested in a sensitive rabbit species that they found -- they found the same effect.

So there can even be species-specific differences that have to be considered, and they can be different between different species.

Q. One does not assume that what happens in an animal is going to happen in a human or vice versa, correct?

A. Yeah, you can't just assume based on a singular dataset. You need to look at the totality of the data, and you build strength when you start to see effects across multiple species, or particularly even across multiple kingdoms in biology when you start to see similar effects. This builds

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strength that a similar outcome will also occur in humans.

Q. Okay. So if you're looking at an outcome in an animal model for ASD or ADHD, what is the most -- most direct, best evidence you can come up with in an animal model?

A. Well, there's two parts to that in my work. And so one is that to look at the behavior, so we have the behavior analysis, then we compare to what's considered as kind of a core set.

And in my work, it's typically compared to valproic acid. So we would compare the core behaviors to valproic acid exposures in the animal.

And then we would also do pathology on the brains of the animals in addition to, if available, functional genomics, that is gene expression studies, or metabolomics to look at the particular active molecules in the brain.

Q. And the behaviors you would be looking for in an autism model are what?

A. So the same core behaviors that

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we might see in humans. So differences in social interactions, repetitive behaviors. And so we're looking for this core set of -- referred to as autism behaviors in the mouse, and there are representative tests for that.

Q. They're very specific in the mouse, though, right?

One is -- the repetitive behavior is grooming, the social behavior is either being around other mice or not. Right?

A. So one example of a social behavior would be referred to as a three-chamber test, or what we call the Jackie box, where the animal -- we see if it prefers or doesn't prefer to be around other animals, which would be a social behavior. And there are different types of social behavior.

And what's currently recommended is to use multiple tests per behavior -- or per core behavior to strengthen the information you have about those behaviors.

Q. And if you're trying to gather

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behavior on an outcome, like ASD and ADHD, after an exposure in a pregnant mouse, studies that are examining effects on adult mice are not directly on point, correct?

A. They may be informative on concentrations or mechanism, but they're not going to be necessarily informative on the outcome, the specific ASD or ADHD outcome.

Q. Okay. Let's talk now about human studies and acetaminophen.

In order for an in utero exposure to happen in a human, the exposure has to first be -- the mother has to take acetaminophen, right? You agree?

There's, like, four steps here. I'll see if you agree with them.

A. So there is some background of acetaminophen exposure in the general population, and it has to do with environmental exposure. And so there's an underlying exposure initially.

Q. Dr. Cabrera, your causation opinion here is focused on women who actually ingest pharmaceutical acetaminophen, correct?

A. That is correct.

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Q. Okay. So the pregnant woman first takes acetaminophen, right? In the mouth?

A. Predominantly. There is also IV indications, but, yes, predominantly.

Q. Your opinion is about pill ingestion predominantly, correct?

A. I haven't been asked for case-specific as far as exposures, but we're -- the exposure happens, and there are currently two routes of exposure commonly. I think there's also a rectal exposure as well, but the majority of them, the vast majority of them, would be an oral exposure.

Q. The human exposure studies where it specified what it was, it was pill ingestion, correct?

A. Predominantly, yeah, it's going to be pill ingestion.

Q. Okay. The first stop is -- where the body takes on any acetaminophen is in the small intestine, correct?

A. As far as absorption, yes.

Q. Absorption.

A. Yes.

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Q. Then it goes to liver, correct, in the mother?
A. Well, in -- yeah, as far as metabolism goes, it goes into a particle, it's referred to as a chylomicron, and then that would end up in the liver.
Q. Okay. Whatever is not metabolized by the liver is now in the blood in the mother, right?
A. Fair enough. It -- yeah. So it's going to go into circulation as well.
Q. Into circulation.
And in circulation, that is the first time it has access to the placenta, right?
A. So within circulation, yes, it would have access to the placenta.
Q. Okay. It has to cross the placenta, right?
A. In order to have access, which we refer to as access in teratology, it would have to cross the placenta.
Q. In order to have access to the baby, we're through the mouth, small intestine, metabolized by the liver, into the

Page 203

bloodstream, it has to cross into the placenta, correct?
A. No. I'd say as far as first or second-pass metabolism, I have to look specifically at that, but that's at least in part correct, yes.
Q. Okay. And then next to actually access the baby, it -- the brain, right, which is what you're talking about in this opinion, it has to cross the blood-brain barrier, right?
A. Acetaminophen readily crosses the blood-brain barrier. So if it has access to the baby, it will have access to the brain.
Q. Right.
All of those things have to happen before it makes it to the fetal brain, correct?
A. That is correct.
Q. Okay. And you haven't -- you've cited various studies, but you haven't cited anything that directly measures the availability of acetaminophen following that exposure route in the fetal brain, correct?

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A. I have looked at fetal brain exposure in the animal models, and I have cited that in my report.
Q. I was talking about human.
A. As we've already indicated, those studies would be unethical.
Q. And all I'm doing, for the record, is clarifying what we have and what we don't.
We don't have any study or data that shows the availability in the fetal brain at this -- at this point in time because of ethics and things like that, fair?
A. Yeah. Just to be clear, I'm fairly sure that's, like, even against the law in Texas. But with that being said, that data doesn't exist.
Q. Right.
A. For any drug.
Q. But we have it in the mouse model.
A. We do have it in animal models.
Q. Right.
All right. I'm going to stick with humans for a while.

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One of the database studies you cite is Avella-Garcia. And that's an autism study, right?
A. Yes, it is.
Q. Okay. And you rely on this to support your causation opinion, right?
A. I have, yes.
MR. MURDICA: We'll mark it as Exhibit 9.
(Cabrera Exhibit 9 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. This one was from -- well, you have in front of you Exhibit 9, right, Dr. Cabrera?
A. Yes, I do.
Q. Okay. And that's the Avella-Garcia study, right?
A. It is.
Q. This is the one you cited in your opinions, fair?
A. I believe so, yes.
Q. From 2016?
A. Looks correct.
Q. Okay. So this was at the point

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that you already formulated an opinion that acetaminophen could cause autism and ADHD, right?

A. As I indicated, there was growing evidence of that since 2015.

Q. I think you said earlier that -- well, correct me if I am wrong. I thought you -- your causation of -- you believed that it was causal as of 2016, I thought you said.

Is that not right?

A. I hadn't done this research in 2016.

Q. Okay. So sitting here today, you can't say when, in Dr. Cabrera's mind, this became causal until -- except for 2023, right?

A. That's when I did the causation analysis. So I couldn't say I had determined causality before then because I hadn't done that analysis.

Q. And you couldn't say anybody could have determined causation before then because you didn't do that analysis, right?

A. Well, I can't offer my opinion

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about what other people did because I'm not other people.

Q. But you, Dr. Cabrera, when I asked you, you -- based on the totality of the evidence that you've reviewed, you can't say there was enough there in 2022, right?

A. 2022?

Q. Yeah.

A. I wasn't looking at the question in 2022.

Q. Right.

But based on what you know today, you -- you're not going to sit here and say there was enough evidence in 2022 for this to be causal, right?

MR. TRACEY: Jim, let me just interrupt you for a second.

Are we doing liability depositions? Because if we are, I'm happy to join with your experts, but I thought this was a general causation deposition.

MR. MURDICA: It is. And that's not what --

MR. TRACEY: So we're going to

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do what we knew and when we knew it?

MR. MURDICA: I'm not doing that. I'm -- Sean, I'm asking him questions about general causation.

MR. TRACEY: No, you're not. You're asking him questions about when anybody could have known that Tylenol caused autism.

I'm happy to play that game with your experts, if you want, but I thought this was a general causation deposition.

MR. MURDICA: Okay. I'm not going to argue on the record with you, but all I asked him to say is he's not going to say when somebody could have known it, and he didn't answer that question.

MR. TRACEY: Well, I know, because he hasn't been asked that question, and he hasn't developed that opinion. That's a phase II opinion. He may very well have that opinion when we finish depositions.

MR. MURDICA: Okay. Well, let

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me try and --

MR. TRACEY: I just -- it just feels like it's part of the phase I.

QUESTIONS BY MR. MURDICA:

Q. Sitting here today, Dr. Cabrera, do you have any opinion on when the relationship, in your view, was causal, one way or another?

A. I only have my personal experience in that when I conducted the analysis, I found it to be causal. I can't say when other people should or shouldn't have found it.

Q. In 2023, correct?

A. That's correct.

Q. Okay. Now, on Exhibit 9, so this was a database study in human beings, right?

A. I'm not sure what you mean by "a database study."

Q. Okay. There were maternal interviews at 12 and 32 weeks during pregnancy, correct?

A. That is correct.

Q. Okay. And there were about

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1,300 participants?
A. So there was 2,644 mother-child pairs. So as a -- as a child outcome, there would be 1,300.
Q. Okay. And if you look at Table 3, which is on page 1992 in the journal, these are the outcomes. And what you cite in your report is for males --
Are you on Table 3?
A. Yes, I am.
Q. Okay.
-- for males with persistent -- that were exposed to persistent acetaminophen exposure which was defined in this study as the mother saying that acetaminophen was used during both interviews, I believe. The score in the right column is a 1.91 from .44 to 3.38, right?
A. Could you repeat the question?
Q. Sure.
If you look under males -- well, let's start with all participants.
Do you see that part, where it says "All participants, never sporadic, persistent," Dr. Cabrera?

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A. Yes, I do.
Q. So if you look at any of those for all participants, the total score is never positive and statistically significant, correct?
A. So that's part of the data. There is significant effects in regards to omission of errors. The total score is not significant.
Q. Okay. And if you look -- then they break it down by sex, right, between male and female children?
A. They do.
Q. Okay. And if you look at males with persistent use, it is -- the effect is -- the score is 1.91, and it's significant, correct?
A. To be clear, it's 1.91, and the odds ratio crosses -- crosses 1. So that would not be reported as significant, although in the omission errors, the risk is 1.56 and that is statistically significant. It does not cross 1 with the confidence interval of 1.09 to 2.24.
Q. Okay. And that's for 21 of the

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1,300 children that are behind that score, correct?
A. You may want to ask that question again.
Q. Sure.
You're looking under males --
A. Yes.
Q. -- with persistent use?
A. (Witness nods head.)
Q. And is 21. That's 21 boys, correct?
A. That's correct.
Q. And then you're looking at the omissions and errors column, and you just cited to use the 1.56 from 1.09 to 2.24, correct?
A. Sorry. That's correct.
Q. Okay. And the -- that data is based on 21 children of the 1,300 participants, correct?
A. That is what it says, yes.
Q. Okay. That's about, what, 1, 1 and a half percent of the study population?
A. Approximately.
Q. When Dr. Cabrera decided how to

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weigh, quote/unquote, evidence like this, did Dr. Cabrera consider miniscule population sizes within a larger study to give credit or discredit to a result like this?
A. I did not discredit the study based on a small number of participants. I considered the totality of data.
Q. Okay. And the totality, with the total score, for all participants, as we saw above, was not significant, right?
A. In regard to the CAST total score, it was still an increased risk at 1.91, but it was not significant based on the confidence interval.
Q. Okay. And that's for males, but with all participants, when you consider males and females, it would -- it would be even more attenuated, right?
A. It was.
Q. Okay. And then if we look at females, and we look at -- let's take, for example, sporadic use of acetaminophen during pregnancy.
Are you with me --
A. Yes, I am.

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Q. -- that row?
And we look at the total score, for 287 female children, the score is -- you didn't like when I used the word "protective," so you could use your own. But it's protective and statistically significant, correct?
A. It was deemed to be statistically significant and with a reduced risk.
Q. Right.
So if we were blindly practicing medicine and relying only on this study and we knew that our patient was going to have a girl, this would indicate we should give sporadic dosing of acetaminophen throughout pregnancy to protect from autism, correct?
A. I would not practice medicine like that. And I hope no one else does either.
Q. Doctor, based on this study and this study alone, in this population, the mothers who were having girls who took acetaminophen actually protected their

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daughters from autism, according to this dataset, correct?
A. There was a decreased risk with sporadic use.
Q. And you just said if you could prescribe medicine, you would not prescribe acetaminophen based on this one number, and that you would agree that applies to any number in any study, right?
A. I wouldn't propose that sporadic use should be used protectively outside of its use to treat fevers, and in which case it very well could provide a protective effect.
Q. And you don't -- you don't make a decision based on one of many findings statistically in a study, correct?
A. To be clear, the expectation is that none of the findings will be significant or, if any, that they would only be whatever the alpha is. So you would expect a false discovery of, say, 5 percent of that data.
And so we consider all of the data under that -- under those understanding.
Q. Right.

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And, in fact, when we look at most of the human data that we have on acetaminophen and pregnancy, it was not collected for that purpose at all, right?
A. I'm --
Q. Did you say right?
A. I don't understand the question.
Q. Okay. Sure. Let me lay a little more foundation for you.
You cited and looked at several ADHD, in particular, but some autism, database studies that looked at pregnancy databases particularly in Norway and the Scandinavian countries, correct?
A. So maybe that's just a difference in definition, but I think of these as -- they're cohort studies.
Q. Okay. Cohort studies.
A. Right. Database makes it sound like their virtual.
Q. Okay. Well, there's a dataset that's based on -- in those countries, it's based on health registries because of national -- you know, public insurance,

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right?
A. I'm familiar, yeah.
Q. Okay.
A. I've done some work with those studies.
Q. Okay. So that data was collected by the -- by the government of those countries not to study acetaminophen, right?
A. Similar to what we do here with National Birth Defects Prevention Study, which we're also a part of, it's a surveillance. It's to surveil a population for adverse outcomes.
Q. And they run and other researchers run tons and tons of analysis across that data because it collects it for everybody because it's a national insurance program, right?
A. I don't know that it collects it for everyone, but it does collect it for everyone that's part of the national health care system.
And it then goes into the system that can be queried in that regard

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and -- but the samples themselves are both archived and analyzed because I've been part of the analysis for those samples as well.

Q. Right.

My point is, right now someone could be running comparisons and studies across that data for tons of outcomes, and we will never hear about them because they turn out to not be anything, right?

A. Well, you're saying if they're negative results -- encouraged to also publish the negative results, but I couldn't say whether they would or wouldn't publish them.

Q. Right.

But by and large what gets published are -- even if there's negative results with them, it's the positive results that people find interesting and that make it into the journals most likely, right, most often I should say?

A. Most often. I think it's common to like headlines, unfortunately.

Q. Right.

And there's a name for that,

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right?

A. What is the name for that? Does it say it here?

Q. Publication bias, right, Doctor? There's a name you -- people who do this use, and it's called publication bias for what we just discussed?

A. Ah, in regards to being more likely to publish positive findings, that there's potential publication bias there. In addition, there's potential publication bias for repackaging results to pile the literature with a particular outcome.

Q. And we see that sometimes with meta-analyses of one or two studies that really just repeat the same thing, but now they're a meta-analysis, right?

A. Well, a specific example we see quite often with clinical studies to try to promote the use of particular medications, this packing of the literature, but there is the potential for it in meta-analysis if you don't consider the same group publishing multiple times.

Q. So the answer to my question

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was "yes," and then you gave me another example of clinical studies, right?

A. I -- that was my answer, so...

Q. Okay. Fine, then I'll ask it again.

Another example of publication bias is that if you have a study finding a positive association and then a second one comes out, that first author sometimes might do a meta-analysis of the two and republish the same thing.

And they'll get published again, and now it looks like there's three studies and a meta-analysis when really it's just still just two studies, correct?

A. Is this a hypothetical?

Q. Yeah.

A. If that happened hypothetically, then it could create some bias in the literature.

Q. Okay. Let's go back to literature.

How important was Exhibit 9 to your causation opinion?

A. I'd say it was a study I

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considered as part of -- part of the analysis, so...

Q. Which number in Table 3 is most significant to you for your causation opinion?

A. So my general question is, are there findings of increased risk in these tables? And I see that there are increased risks, particularly with persistent use in omission errors.

So that would be a finding that's consistent in the different groups in omission errors.

Q. And how do you balance that with the lack of findings in several of these results and the opposite findings, the protective findings?

A. So in regards to the CAST score in particular, it's simply a matter of is -- are we consistently finding negative or decreased risk in multiple studies, if you wanted to say that there was a protective effect. We could look for the same thing, and so to consider that also, so...

Q. Right.

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So if you only had this paper, Exhibit 9, would you say that acetaminophen causes autism in human children?
A. I would say it was still unclear.
(Cabrera Exhibit 10 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Let's take a look at another one.
Okay. Dr. Cabrera, I've marked and put in front of you Exhibit 10, and I'm going to represent to you that it's a Ji study from 2020.
Do you have it?
A. I do, yes.
Q. Are you familiar with it?
A. Yes, I am.
Q. Do you rely on it in your report?
A. Yes, I do.
Q. Okay. Now, in Dr. Cabrera's world, how important are cord blood studies?
A. It can be very important.
Q. Okay. And where do they fall

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in your hierarchy of evidence?
A. If supportive, they provide strong evidence.
Q. Okay. And do all cord blood studies only capture the peripartum period of time?
A. Well, it could be pre or peri in regards to cord blood, depending on when the medication was administered.
Q. The cord blood studies that you're aware of are taken around the time of birth, though. This is not like a genetic testing in the first 15 weeks tests we're talking about, correct?
A. So the collection of the cord blood itself is perinatally, during delivery.
Q. That's what I was asking you originally.
Okay. So what would be in the cord blood would reflect -- depending on the half-life of whatever we're looking for, it would reflect what was in the cord -- or what the cord was exposed to around the time of delivery, correct?
A. Preceding delivery.

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Q. Preceding delivery, okay.
But immediately or close to that preceding delivery depending on the half-life of whatever is being studied, right?
A. As a function of the half-life.
Q. Okay. And you looked at the study already, right?
A. Yes, I have.
Q. Okay. And was the cord blood in this study collected specifically to study acetaminophen?
A. Well, initially -- I don't know that they were initially. I'm looking for that, so...
Q. Okay. Do you know how often the mother's exposure to acetaminophen during the pregnancies that resulted in the cord were collected?
A. Could you repeat that question, please?
Q. Sure.
Ultimately for however many -- so not everyone who was enrolled in this dataset ended up having harvested cord blood,

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correct?
A. That is correct.
Q. Okay. Only about a third actually had their cord blood harvested that had been enrolled, correct, a little less than a third?
A. To be clear, the math again is mother-infant dyads at 3,163, so...
Q. You're right. It's more like two-thirds, not one-third, fair?
A. I -- yes, that's -- closer to two-thirds, yes.
Q. Okay. And what measurements were taken throughout the pregnancy as to exposures to different medications?
A. So the information that they include in the study includes maternal age of delivery, maternal race and ethnicity, maternal education level, maternal status, stress during pregnancy, smoking before or during pregnancy, alcohol use before and during pregnancy, maternal BMI, parity, child sex, delivery type, preterm birth and low birth weight.
And then there's additional

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stratification, but I don't see specific indication about other medication.
Q. Right.
Dr. Cabrera, they never asked the mothers who -- whose cord blood was sampled here whether they -- whether they took acetaminophen ever once or how often, correct?
A. I -- my understanding is, as indicated in my report, they did not ask. They measured for acetaminophen in the cord blood but didn't correlate that with a recall.
Q. Right.
And another way -- so they didn't ask the mothers if they were exposed to acetaminophen. They also didn't ask them when they were exposed to acetaminophen, correct?
A. That is my understanding.
Q. Okay. So the only thing we have from Exhibit 10 is this one snapshot of time right before delivery, correct?
A. Well, we have acetaminophen exposure or documented acetaminophen

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exposure.
Q. Only at this one period, small window of time at the very last hour of pregnancy, correct?
A. I disagree with that. It's not the very last hour --
Q. Okay.
A. -- but preceding pregnancy based on the half-life, which is a few hours.
Q. Okay.
A. And so the expectation is within -- it would be reasonable to say half a day of an exposure beforehand.
Q. Okay. And I asked you before if this was intentionally -- if this study was intentionally done to study acetaminophen.
Do you now -- do you now agree that it was just done to study any metabolites in cord blood?
A. Based on the study criteria initially, it was to look at metabolites in cord blood.
Q. Right.
So this is -- this is one paper

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that came out of this study, but you know that many other things were studied other than acetaminophen, right?
A. They did study other things --
Q. Okay.
A. -- in this cohort.
Q. And you just said, you know, it's probably a snapshot of the -- of the half a day before delivery.
They didn't ask the mothers whether they took acetaminophen for the initial pains of labor, right?
A. As far as I know, there -- they didn't ask the mom about medication usage in regards to acetaminophen.
Q. And you know that -- well, you haven't experienced personally, I assume, but you know that labor is painful, right?
A. I -- I've been told.
Q. You know that one indication for acetaminophen is pain, right?
A. I'm aware of that.
Q. Okay. Wouldn't you expect, based on those two facts, that some women would have acetaminophen in their cord blood

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because they took acetaminophen shortly before they went to the hospital or on their way to the hospital until they got proper pain management?
A. To be clear, if it was a -- that would be something similar to a random effect error. You wouldn't expect to find a dose-response with an outcome.
Q. Well, I just --
A. Something like a random effect error. A random exposure.
Q. Sure.
Oh, and we're going to get to that. I'm just asking you as a logical-thinking, breathing human being who knows a little something about the real world, would it surprise you if mothers were taking acetaminophen for the pains of labor before were properly treated as a -- at a hospital?
A. If they didn't know the potential risks, then I could understand them taking it to help with the pain.
Q. And if somebody takes acetaminophen because of the pain of labor on

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the way to the hospital, what scientifically does that tell you about days in their pregnancy that they took acetaminophen for other reasons?

A. Scientifically you can only draw assumptions about their behavior prior to that.

Q. Right.

We really know nothing other than this one snapshot, right?

A. Quantitatively, we don't know behaviors prior to that.

Q. Okay. By the way, we're talking about cord blood now, but on your -- on Dr. Cabrera's hierarchy, is a cord blood study better or less good than a meconium study for looking for pregnancy outcomes like this?

A. The, I think, meconium study is better.

Q. Okay. All right. Let's get into this a little bit.

On Table 1, which is on journal page 184. Let me know when you're there.

A. I'm -- Table 1, yes, I'm there.

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Q. Yeah.

So what this is showing is for the 998 mothers who had their cord blood taken, this is some of that background information on basically demographics, right?

A. Yes. So it's -- Table 1 is titled "Maternal and child characteristics according to child physician-diagnosed conditions."

Q. Right.

And for -- let's look at something like preterm birth.

Are you there?

A. Yes.

Q. Okay. So the babies who were born preterm have more than double rate -- actually, sorry.

The babies who were born preterm, about 20 percent of them had ADHD and 28 percent had autism, right?

A. So 28.8 percent had ASD, autism, and 20.6 percent had ADHD.

Q. All right. And that's increased over the first column, right? The first column is what? It's no developmental

Page 232

issue, right?

A. Yes.

Q. Okay. So no developmental issue, only 8.9 percent of them were born preterm, right?

A. That's what it says, yes.

Q. And then for developmental issues, for ADHD and ASD in particular, you know, one is double, ADHD is double the amount of the percentage of preterm birth, and ASD is triple, correct?

A. Approximately.

Q. Right.

And you'd expect that, wouldn't you? Because you know that preterm birth is one risk of developing ADHD and autism, right?

A. There are potentially neurodevelopmental impacts from a preterm birth.

Q. Okay. And in Dr. Cabrera's opinion, are those causal, or are those still under investigation?

A. In what capacity?

Q. Is preterm birth something that

Page 233

can be causally associated with ADHD and autism?

A. I'd say those are associated. I don't know that one causes the other.

Q. Okay. Is that because you haven't done a full Dr. Cabrera analysis on it yet?

A. Because as far as I know in the literature, there's association, and I haven't done the analysis either.

Q. Okay. And association is not causation, right?

A. Association in itself is not sufficient for a causation.

Q. Okay. Let's look at maternal smoking during -- before or during pregnancy.

Do you see that? It's about halfway down the column.

A. Yes, I do.

Q. Okay. And for a continuous smoker, somebody who smoked throughout pregnancy, do you see that about 4 percent had no neurodevelopmental issue, 9 percent had ADHD, and 10.6 percent had autism, right?

A. That is correct.

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Q. So smokers had a significant increase in ADHD and ASD as a proportion -- as a percentage, right?
A. There was a significant difference in regards to smoking --
Q. And --
A. -- and the outcomes.
Q. And that's not a surprise to you because you know that ADHD and autism are caused by smoking, right?
A. I would say that there's -- there is an association with smoking and autism.
Q. Okay. So it's the same answer. There's an association, but you don't know for sure that a mom smoking throughout pregnancy causes autism or ADHD?
A. I haven't personally done a Bradford Hill on that, but in regards to smoking, smoking has been contraindicated during pregnancy as associated with various neurodevelopmental and congenital outcomes.
Q. Okay. But you're not ready to attribute causation yet, right?
A. Well, I would say it's a risk

Page 235

factor.
Q. Okay. It's a risk factor.
In Dr. Cabrera's opinion, is acetaminophen more likely to induce autism in a pregnancy than continuous maternal smoking?
A. I would say if you wanted to analyze the risk of autism, you should adjust for maternal smoking as another risk factor because you wouldn't want to influence the outcome.
So independently, I haven't compared them quantitatively with each other.
Q. But you're going to -- you will stand up and you will tell the judge in this case that acetaminophen causes autism, but you won't stand up and say that continuous smoking during pregnancy causes autism?
A. I would say that there -- they -- you have to modify as -- is it a risk factor for causing ADHD and ASD if you're analyzing autism. And I'm simply saying I haven't -- I haven't done, nor have I seen, a Bradford Hill on smoking and autism or ADHD as an outcome. I'd have to look at that specifically.

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I haven't -- I haven't asked, and so I can't answer that question.
Q. But that's not defending war criminals, right?
A. So Philip Morris isn't in the room, so that's -- it depends on who you ask.
Q. All right. Let's go on to Table 2.
Let me know when you're there.
A. I'm there.
Q. Okay. So what Ji did is took that -- took the acetaminophen metabolite level in the cord blood from that one snapshot in time at delivery, correct?
A. They're analyzing the cord blood that was collected during delivery.
Q. And in particular, they're analyzing it for acetaminophen, right?
A. Acetaminophen and metabolites of acetaminophen.
Q. Right. Right.
They're using the metabolite as a proxy for acetaminophen, right?
A. Yes. And it's important to note the metabolites also have a longer

Page 237

half-life than just acetaminophen as well.
Q. Okay. How much longer? Are we talking days?
A. Days.
Q. Weeks?
A. Weeks is probably farther out than the metabolites would be expected, but some of them may be within weeks, not longer than that.
Q. Okay. And then what Ji did is, depending on the measurement of the cord blood acetaminophen metabolites, broke it into three groupings. Basically took every -- all 998 measurements, and not everyone had acetaminophen, right?
A. Yes.
Q. Okay. Took the ones that did, put them all in order, right, from least to most or vice versa, and broke it into three groups, right?
A. So it's referred to as tertiles. They've done an analysis and split the group into three based on where they fell within the group.
Q. Right.

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But they were even groups. It's not like there was a threshold for one group and a threshold for another. They just broke it into three groups, right?

A. Well, it's a -- how distributions work, you can just apply a cutoff, and you end up with thirds based on the distribution of a normal distribution.

Q. Right.

But it wasn't like we're going to ignore this group that has -- that has the low level or anything like that. It was just three even groups, right?

A. So the group defines what a low level is.

Q. Okay. And it was broken up into three levels, right? The third tertile just meant the high -- the grouping of the highest levels of cord blood acetaminophen metabolite, right?

A. Yeah. So they're grouping based on the tertiles, and the third group appears to have the highest exposure.

Q. In terms of the cord blood measurement, right?

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A. Yes.

Q. Okay. So the third group had the highest exposure for whatever snapshot in time the cord blood was able to capture around -- right before delivery, right?

A. Yes.

Q. Okay. And so then if we look at some measurements, the first tertile, that ended up being our control, right?

A. Yeah, they're giving that a measure or odds ratio of 1, so that's our -- becomes our control.

Q. Right. And then so then we look at the second and third tertile.

And so let's look at, for example, the first piece of data in here. It's ADHD and -- in the second tertile for unchanged acetaminophen.

And that is not statistically significant, correct?

A. It's an increased risk, 1.48, but it does cross -- it does cross 1.

Q. Okay.

A. In regards to the confidence interval.

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Q. And that alone, even Dr. Cabrera would not say that that is evidence that you would rely on that ADHD causes -- or sorry, that acetaminophen causes ADHD, correct?

A. Well, to be clear, that's one part of this data.

Q. Yeah.

A. And so if that was the only part, I would say that it would still be unclear. But that's -- it's not the only part. There's also the third tertile where there's -- where the risk continues to go up, and that's where we see this concentration-dependent effect or a dose-effect with risk.

Q. Yeah.

And so I said that alone, and you wouldn't rely on that alone. And don't worry, we're going to go through all of these.

So back to that second tertile number. The .92, the way statistics works is it could very well be that the actual data there is that the risk effect is .92 below

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the null, correct?

A. There's a miniscule possibility that it could be 0.92 based on the variation of the point estimate.

Q. Well, these are statistics. So define "miniscule."

A. Well, the distribution is the point estimate of 1.48 is the central tendency. So that's where you would expect it to be.

Q. Right.

A. The further you get away from that, the less is the likelihood that those numbers represent what the point estimate is; that the point estimate is the central tendency.

Q. Right.

And it very well could be there's a -- there's a small possibility that it's 2.39, but there's an equally small possibility that it's 0.92, correct?

A. Within the variation, those are possibilities.

Q. Okay. And if we look over to the next column, for autism, and unchanged

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acetaminophen in the second tertile, we see something similar, right? 1.32, but not statistically significant, correct?

A. I see 1.33 for the adjusted odds ratio.

Q. Oh, I have a pen mark over mine. So thank you.

So then if we go down to -- and then there's -- Dr. Cabrera, there's other measures for the metabolites, right?

A. Yes, there are.

Q. And there's data reported for each of those, right?

A. Yes, there are.

Q. So, for example, under glucuronide, one of the metabolites, if there was -- if it was detected -- and it was only detected in 192 of them, right?

A. Yes. Any detection, 192.

Q. They didn't break this down into tertiles because the numbers were too low, right?

A. Well, because there's -- there was a no detection and any detection, and so they broke it down that way.

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Q. Because only 192 had any detection. So they didn't break it up because the numerosity wasn't high enough, right?

A. Oh, in regards to tertiles?

Q. Yeah.

A. I can't say the decision on why they didn't break it into tertiles other than the fact that they had a what's referred to as an unexposed group that was no detection.

Q. Okay. And if you look across to -- they also measured ADHD and ASD together in the same patient, right?

A. They did group them.

Q. So in the third column for that, when there's some detection of this metabolite, it was, again, 1.55 from .053 to 4.15, not statistically significant, right?

A. So to be fair, the adjusted odds ratio for ADHD was significant with an increased risk of 2.25.

And the adjusted odds ratio for ASD was also significant for 2.29, but ADHD and ASD, the adjusted odds ratio was 1.55, and it did cross 1. Also an increased risk,

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but it was -- it could be considered not statistically significant.

Q. Right.

And, Dr. Cabrera, just to make this easier, the plaintiffs' counsel is going to have an opportunity to ask you questions after I'm done, so you're going to get to talk about all the things that you think support your opinion, if I forget to ask you about them or choose not to.

Okay?

If you go down to cord acetaminophen burden, you understand that to be a measure of the unchanged acetaminophen, the glucuronide and the acetyl cysteine metabolite as well, right? The three that they measured?

A. The N-acetyl cysteine metabolite?

Q. Yeah.

A. Okay. I'm looking at that. Do you have a question about it?

Q. So -- sorry. We're down in the last section of rows where it says "cord acetaminophen burden"?

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A. Okay. Yeah. So you're -- okay. We're skipping over N-acetyl cysteine?

Q. Yeah. Yeah, my -- I mean, we can -- we can do it if you want, or you could do it with your counsel later, but I was just going to ask you about the total acetaminophen burden.

And my question for you, and I think we got a little confused there, is the total cord acetaminophen burden is all of -- it's the two metabolites they measured plus pure acetaminophen, right?

A. My understanding, they are looking at all of the metabolites of acetaminophen in that regard. Total burden.

Q. Okay. And if we look in the second tertile for autism and autism and ADHD together, we have positive point estimates that are not statistically significant, right?

A. In the second tertile?

Q. Yes. For ASD and ADHD with ASD.

A. Okay. So just to be clear, the points there for ADHD, there's a significant

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increased risk for ADHD of 2.26, that's significant statistically; an increased risk or odds ratio of 2.14, that is not statistically significant; and then for ADHD and ASD, the odds ratio is 2.1, and it would be considered not statistically significant.

Q. Okay. And in the third tertile, if we look over to ADHD and ASD together, the point estimate is positive, but that one is not statistically significant, correct?

A. And, again, for -- to cover all of the data --

Q. Doctor, your counsel --

A. -- the third tertile --

Q. Your counsel's going to --

A. -- in the ADHD is 2.86, and it's statistically significant. For ASD, it's 3.62, and it's statistically significant. But for ADHD and ASD, it is also an increase odds ratio, but it was not statistically significant. But it was an increased odds ratio of 2.44.

Q. Okay. And, Doctor, when you were looking at this, did you -- were you

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able to figure out the percentage of the cord acetaminophen burden that was the metabolites versus the unchanged acetaminophen?

A. As far as I know, I didn't see a -- quantitative values for them.

Q. It's not reported, right?

A. I haven't seen that data.

Q. Okay. So you don't know, for example, for ADHD in the second tertile for unchanged acetaminophen, it wasn't statistically significant, but when considering the total burden, it was, correct?

A. Can you repeat the question, please?

Q. Sure.

For ADHD -- for the outcome of ADHD --

A. Okay.

Q. -- looking at the second tertile, for unchanged acetaminophen, there was no statistically significant effect, but for total acetaminophen burden for the second tertile and ADHD, there was, right?

A. That is correct.

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Q. Didn't you wonder what changed, which metabolite -- what was the burden of the other two metabolites?

A. Inasmuch as we can see that both of the other metabolites showed an increased risk when they were detected, or an increased odds ratio when they were detected for ADHD, it appears that they were driving -- that is, those longer-lived metabolites are -- were driving that increased risk.

Q. On a very -- on a comparatively small number of patients, right, compared to the unchanged acetaminophen?

A. Well, it's still the total number in the second tertile with the cord acetaminophen burden, but it appears to be enough to move the odds ratio to an increased risk.

Q. Have you -- have you talked to -- do you know Yuelong Ji?

A. I do not.

Q. You've never communicated with Yuelong Ji?

A. I did not.

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Q. Okay. So you didn't ask any questions about this study, I take it?

A. I have not asked -- I have not been in communication with the authors.

Q. Okay. Did you presume, Dr. Cabrera, that this -- that the acetaminophen present in the cord blood at the time of birth, did you extrapolate that in your causation analysis to the entire pregnancy of this dataset?

A. To be clear, I took it at face value in that it shows a concentration-dependent or referred to as a dose-dependent increase in risk.

Q. Which could be eliminated, corrupted or completely attenuated in the circumstance I described where a woman was taking acetaminophen for the pains of labor, right?

A. Well, you wouldn't expect that to result in an increased risk that was dose-responsive in that regard.

Moreover, the fact that there's also increased risks associated with the longer-lived half-lives of the other

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metabolites, including the glucuronide and the N-acetyl cysteine, which is, at least in specific cases, would be indicating that it interacted with glutathione and that it's actually -- you're detecting acetaminophen and glutathione in the newborn's cord blood.

Q. Did Ji say that in the study?

A. I'm familiar enough with the biochemistry to understand that.

Q. You've testified before that weeks 2 to 4 of the human pregnancy are the most sensitive to neurodevelopmental outcomes like autism and ADHD.

Do you recall that?

A. Specifically for neural tube defects, those are the sensitive window for neural tube defects.

Q. Okay. You have no idea for this dataset what acetaminophen, if any, each of the 998 mothers took during weeks 2 to 4 of their pregnancy, correct?

A. Can you clarify what acetaminophen, if any?

Q. Well, yes. I'll rephrase.

Dr. Cabrera, for each of the

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998 women whose cord blood were measured in the study, you don't know if they took acetaminophen in weeks 2 to 4 of their pregnancies at all, correct?

A. I have no way of determining whether they took medication during the first trimester of pregnancy.

Q. You don't know if they were exposed to acetaminophen during any of the -- of the relevant periods of brain development that even you would testify to, other than this one day before they gave birth, correct?

A. I would say this data is actually most consistent with a third trimester exposure. I wouldn't be comfortable saying that it included any exposures before that.

Q. You only know that they were exposed one time within six to eight hours before the cord blood was taken, right?

A. In regards to the unchanged acetaminophen, that is the correct assumption.

In regards to the metabolites, as I've already indicated, the metabolites

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have a longer half-life, and those wouldn't be on the order of hours. It would be days.

Q. Right.

And if they -- if the exposure was days for the longer half-life, it would be at a very low dose because days before it would be depleting as the half-lives went, right?

A. Not necessarily inasmuch as there's evidence and -- not yet in humans, but in, I believe, the ewe, which is a -- lamb studies, that showed that these metabolites may actually be circulating in the uterine environment and swallowed and then recirculated by the -- by the developing fetus.

They can actually by and large accumulate there.

Q. That's a -- that's a hypothesis, correct, Dr. Cabrera?

A. That's -- it hasn't been shown in humans, but it has -- it has been shown that those metabolites are found in lambs.

Q. Okay. Understanding that they've been found in lambs, Dr. Cabrera,

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you're not going to testify in front of this Court that that's a mechanism of action here that you could say with certainty, correct?

A. I can't say that it works just like that in humans. There's a study on it in lambs.

Q. All right. If you turn to page 187 of this, we're under Limitations.

You see the Ji identified what we're just talking about, that a limitation is that it was only a one-time measurement of acetaminophen, and it at most reflects maternal use -- may at most reflect maternal use of acetaminophen during the peripartum period.

You agree with that, right?

A. As I indicated for free acetaminophen, that's -- that is correct.

Q. Okay. And Ji doesn't say anything else about the metabolites, other than what I just read to you, right?

A. Not that I've read in the study.

Q. Okay. And one other thing that Ji says is that liver is the primary location

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for metabolite -- metabolism of acetaminophen.

And you don't disagree with that, right?

A. The predominant -- the majority of acetaminophen one consumes would be metabolized by the liver, which is why there's increased risk for hepatotoxicity.

Q. Okay. And one more question on this, and then we can move on.

Yeah, we can take a break.

Back on page 181, Ji notes in here -- and this is in 2020 he's noting this. The American Academy of Pediatrics grand rounds concluded there's no definitive causal link between acetaminophen exposure and ADHD. That was in 2020.

I take it you disagree now with the American Academy of Pediatrics, right?

A. You didn't tell me exactly where you're reading that from.

Q. Oh, I apologize, Dr. Cabrera. I use my finger-pointing right here.

A. Okay. All right.

Q. My question to you is, you

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disagree with the American Academy of Pediatrics as reported by Dr. Ji here, right?

A. I -- inasmuch as this is part of the introduction, they're saying prior to this study that the American Academy of Pediatrics grand rounds concluded that there was no definitive causal link between acetaminophen exposure and ADHD.

MR. MURDICA: Okay. We can take a break. Thank you, Dr. Cabrera.

VIDEOGRAPHER: Off the record, 2:21.

(Off the record at 2:21 p.m.)

VIDEOGRAPHER: The time is 2:41 p.m. Back on the record, beginning of Media 5.

QUESTIONS BY MR. MURDICA:

Q. Welcome back, Dr. Cabrera. Are you ready to proceed?

A. Yes, I am.

Q. Okay.

MR. TRACEY: How about sound? I need the sound on.

MR. MURDICA: Oh, I'm muted. All right.

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MS. KING: How's that?

MR. TRACEY: Yeah, that's good. It was nothing. Now it's something.

MR. MURDICA: I tried. Didn't work.

QUESTIONS BY MR. MURDICA:

Q. All right. Dr. Cabrera, are you ready to proceed?

A. Yes, I am.

Q. Okay. Earlier this morning when we talked about the various reports you've submitted, two of them were your original report, and then the amended report you submitted a week later.

Do you remember those questions?

A. Yes, I do.

Q. Okay. And your testimony was that you made some typographical changes but nothing substantive, right?

A. That's correct.

(Cabrera Exhibits 11 and 12 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Okay. Marked as Exhibit 11 and

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12 are your original report and your amended report.

Do you have those in front of you now, Doctor?

A. Yes, I do.

Q. Okay. What I'd like you to do is turn to page 135 in the original report, which is the taller stack.

A. Okay.

Q. Okay. Let me know when you're there.

A. I'm there.

Q. Okay. You have a section, weight of evidence for the APAP, ASD studies?

A. Yes.

Q. Okay. And then you have a chart on the next page.

A. Yes.

Q. Do you see that?

A. Yes.

Q. Okay. Now, I want you to open the amended report to the same section --

A. Okay.

Q. -- which I think is -- you got it?

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A. Yes.
Q. Okay. In the chart on the amended report, is the Saunders study in there?
A. I do not see it.
Q. Is it on the original?
A. I -- yes, it is.
Q. And in the original, it's in the chart, and then if you look at the text following it, turn -- if you turn the page --
A. Oh, yeah.
Q. -- there's a description of Saunders as well, right?
A. Yeah, I think it was a -- it was a typo because there's not a description of Saunders.
Q. Okay. Dr. Cabrera, Saunders didn't help you, right?
Saunders found no correlation between acetaminophen exposure and autism, correct?
A. Well, it's two different questions. Which one do you want me to answer?
Q. Okay. How about this? I'll

Page 259

start over.
Saunders found no correlation between acetaminophen exposure in utero and autism, correct?
A. They did not.
Q. Okay. And you had it in your original report, correct?
A. Yes, it was.
Q. And then it is -- it is not in your current report, correct?
A. That's correct.
Q. Okay. And you only made typographical changes in your amended report, correct?
A. Yes. And to clarify, the information that's listed there with Saunders is not the correct Saunders information, so that's why it was removed. That is, the information that follows Saunders is not Saunders information.
Q. Okay. What is it?
A. I believe that's actually a spillover from Liew.
Q. Okay. So Saunders 2019 shouldn't have been in there from the start?

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A. Yes, exactly.
Q. You weren't cherry-picking data and realized you didn't like it?
A. It wasn't about cherry-picking data. It was just that the -- when I was formatting the table, that should have been a Liew citation with a hyperkinetic syndrome, and it ended up being a Saunders.
Q. And somehow the word "Saunders" just showed up there?
A. Well, I was reviewing the Saunders work as well, and that's how it ended up in the table.
Q. So it turns out Saunders is not considered in your weight of evidence, correct?
A. It was part of my analysis.
Q. It was?
A. Yes.
Q. But now it's no longer in the section on weight of evidence?
A. Well, no longer in that they didn't have a significant increase in risk in that section.
Q. So because they didn't have a

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significant increase in risk, it wasn't included in your weight of evidence?
A. It was part of the weight of evidence.
In regards to that particular study, it was referencing the wrong study, and so that's the reason why Saunders was removed.
Q. Do you recall any other substantive changes you made in your amended report?
A. That wasn't substantive --
MR. TRACEY: Objection to form.
THE WITNESS: It was the fact that it wasn't referencing the right material too.
QUESTIONS BY MR. MURDICA:
Q. Do you recall changing your description of Baker 2020?
A. There -- for the tables, there were other editorial typos in the tables that I had to correct as well.
Q. Okay. But it included substance, right?
A. Well, you know, inasmuch as the

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name was referencing the wrong study or the study didn't match the reference, those had to be corrected. There were, you know, editorial changes because it -- basically I typed the wrong name there.

Q. And now I'm asking you about something different now, Dr. Cabrera. You also made changes, additions, substantive additions, in your description of the meconium study, right?

A. I mean, if we want to look at those particularly, we can discuss them.

Q. I'm asking if you remember.

Do you remember that?

A. I did make some other changes in regards to similar problems with the tables that I had to correct.

Q. Okay. You don't recall making any other changes than to two tables?

A. I just said I had to make similar changes to tables that --

Q. Right. Sorry. You know what, that was a poor question.

Other than changes to tables, you don't recall making any other substantive

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changes in your amended report.

Is that fair?

A. I didn't make substantive changes. It was -- these were typos on my part where I had referenced the wrong study with the wrong data.

Q. Okay. You can put those aside for now.

Oh, you know what, while you have it, turn to page 136 in the original report. Where's the current report? This is the original. Where's the current? This is the current?

Okay. If you -- in your description -- in your original report, Exhibit 11, on page 138, you have a description of Baker, right?

A. Yes.

Q. Okay. And then in your amended report, on page 138, you have a description of Baker.

Right?

A. Yes.

Q. Okay. Now, if you look at the third paragraph from the bottom of your

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description, right above results, you don't have anything -- or sorry.

Do you see the limitation section?

A. On 138?

Q. Yeah, in your original report.

A. Yes.

Q. Okay. Compare that to your amended report.

A. I did add additional information regarding the meconium.

Q. Okay. So that was -- that was not an adjustment to a table, right? That was a substantive change, Doctor.

A. Well, I don't know about substantive. It was just to define what the exposure in meconium represents.

Q. It would also offer as an opinion about what meconium can capture, correct?

A. Well, it's more or less by definition of what meconium has been reported to capture, but I didn't include a reference in that regard. It's just generally understood.

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Q. It's not -- was not -- was not a typo and was not fixing a table with a typo, correct?

A. That is correct.

Q. Okay. All right. Let's move on.

In study design, one thing that can account for something like genetics, which here is -- well, you agree that for ASD and ADHD, genetics is, even you'd agree, the predominant influence on the outcome, right?

A. It depends on the case.

Q. Okay. It has 80 to 90 percent inheritability, right, both ASD and ADHD?

A. In twinning studies, there have been some studies that have reported inheritability as high as 80 or 90 percent.

Q. Okay. One way in a study design to account in a situation like this where you'd expect a large genetic component is to have sibling controlling, right?

A. That is a potential study design for controlling such things.

Q. And one sibling would have been exposed to an outcome -- sorry, to an

Page 266

exposure. The other would not have. And you see if they end up having the same or different outcomes, right?

A. So based on what's referred to as discordant siblings, you can perform an analysis that way.

Q. Yeah.

And you looked at a study that did just that with respect to human beings and ADHD, correct?

A. I did.

Q. And what's it called?

A. It was -- I assume you're referring to the Gustavson study.

Q. I am.

MR. MURDICA: We'll take -- we'll mark it as Exhibit 13.

MR. TRACEY: What exhibit number?

MR. MURDICA: 13.

(Cabrera Exhibit 13 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Now, Dr. Cabrera, this dataset, the same dataset had previously been examined

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by the same authors and found an association between ADHD and acetaminophen exposure in the Norwegian health care database, right?

A. Yes, they have.

Q. And this Gustavson study incorporated a sibling control design like we just discussed, right?

A. This study did, as did the previous study.

Q. And when -- and the previous study, you're referring to Ystrom, right?

A. Yes.

Q. Okay. And in Gustavson, when the sibling control was looked at, the effect of acetaminophen in correlation with the outcome of ADHD was completely attenuated or went away in layman's terms, right?

A. So to be clear, under the -- long-term exposure was associated with a twofold increased risk of ADHD diagnosis, and the adjusted hazard ratio is 2.02, statistically significant.

In the sibling control model, the association between long-term acetaminophen use and ADHD in the child was

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an adjusted hazard ratio of 2.77, was statistically significant.

At the between family level, the -- and adjusted hazard ratio of 1.06, which was not statistically significant, the confidence interval was 0.51 to 2.05 at the within family level.

Q. Right.

And you agree that a sibling -- a sibling -- a controlled study is better than an uncontrolled study, right?

A. I generally teach the controls -- having controls is important for studies.

Q. And sibling control in pregnancy outcomes is one manner of control, right?

A. That is an approach to doing these studies.

Q. Okay. And that result, even to the authors here, was surprising, right?

MR. TRACEY: Object to form.

THE WITNESS: What do you mean by that result?

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QUESTIONS BY MR. MURDICA:

Q. Did the -- when sibling control was applied, even though in Ystrom, it didn't attenuate the effect. In Gustavson in the same database on the same data with it just more updated, it did, right?

Would you like me to --

A. My reading of this is they indicate that these results must be interpreted with caution and need to be replicated in other studies.

Q. And while we're on that topic, replication is one of the most important things you can have when trying to determine a causation of an effect to an exposure, correct?

A. Just to clarify, replication is important, yes.

Q. Okay. Isn't that one of the things you most try to do in order to prove an effect?

A. Generally in science you expect results to be repeatable.

Q. Right.

Okay. And so if you look at

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Table 2 on page 7 of 10 of Exhibit 13, you would see that when you look at acetaminophen use of 29 days or more and its correlation with ADHD, it was 2.02, and it was significant, right? That would be the fourth column over.

Model 2 -- you can look at model 1 unadjusted or model 2 adjusted. Both found a positive correlation or an association that was significant, right?

A. They're both reporting a significant increase --

Q. Right.

A. -- in the hazard ratio.

Q. And then if you look at the -- when sibling control was applied in the next column over, regardless of the number of days acetaminophen was used during pregnancy, the -- there's no effect, and it's not significant, right?

A. When they controlled for family effect, the hazard ratio was 1.06 and was not significant.

Q. And if you look at the two rows above that, for lower durations of use of

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acetaminophen in the pregnancy, it's the same, right? There's not a positive effect, and it's not significant, right?

A. That is correct.

Q. Okay. And that, to a geneticist or somebody who speaks about genetics like yourself, when you have a complete attenuation of a large -- a statistically significant effect by applying sibling control, that speaks to this being a genetic -- a genetic cause, does it not?

A. It does not specifically speak to that. And there's multiple reasons for that.

To begin with, when adjusting for these sibling control, you're only adjusting for those factors that are shared. You're not adjusting for those factors that may be unshared, and it's one of the weaknesses with these studies.

Q. Okay.

A. So unshared environmental factors between the two individuals that are discordant is a problem because you're missing them.

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Q. Well, we know of siblings, right -- if you look at a pair of siblings, or a dyad or triad or whatever you want to call it, we know in this study what was looked at was one that was -- the same mother, right? This was not an adoption study?

A. (Witness nods head.)

Q. They both had the same mother, correct?

You've got to say it for the transcript.

A. Yes. My understanding is they both have the same mother at least.

Q. One was exposed to acetaminophen during the pregnancy, and one was not, correct?

A. So to be clear, that's based on the reporting. Even that is a problem with the sib-pair design in that it's more likely that the exposure would be both, but they're reported as discordant. And that's potential grounds for error as well in these studies.

Q. Every study that you rely on in your analysis, Dr. Cabrera, relies on

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reported acetaminophen usage, does it not?

A. That is correct, and that generally biases towards the null. And so the criticism there is actually that that would bias the study toward the null. In all of those studies as well.

Q. According to Dr. Cabrera.

A. According to statistics and epidemiology.

Q. Everybody who reported acetaminophen usage in the studies was doing so based on memory, correct?

A. I mean, could have been an app on their phone. I don't know exactly what their recollection was based upon. A lot of them are referred to as recall. So however manner of recall that they used to recall what they had taken previously.

Q. And like this study, they generally lump the days together into the number of days' use without regard for whether it was at day 47 or day 90 of pregnancy, right, or later?

A. As far as the exposures go, they lump, you know, 1 through 7 days and 8

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through 28 days together and then more than 29 days together.

Q. And you, Dr. Cabrera, as a teratologist, would be much more interested in data that actually identified the days and the lengths of exposure for each particular day in pregnancy, correct?

A. The -- I would like -- I would like data that showed the particular time during pregnancy and what's also referred to as dose and duration as well. And so --

Q. It would be much more -- oh, sorry, go ahead.

A. And so this is showing duration but not necessarily the dose during that duration.

Q. And most -- if we looked at every study in your report that evaluated human data, most of them -- not all of them, but most of them did just this, right?

A. That is to say other studies also reported dose based on duration.

Q. Right.

And it would be much more illuminating for you as a teratologist to see

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exactly what the pregnancy was exposed to at the exact morphological time of the embryo, correct?

A. I would say it would be more informative to have both dose and duration, but duration is -- can also be considered a dose in that it's a longer period of exposure.

Q. Right.

But seven days, Dr. Cabrera, if it was, you know, pregnancy day 3 to 4 and then not again for four months for one day and not again for three months for one day, that's not really meaningful to you as a teratologist, right?

A. When the seven -- or one to seven-day exposure occurs would also be informative.

Q. Right.

Okay. So back to the sibling control. You are criticizing the sibling control design, but it's better than no control, right?

A. Well, if you're overcorrecting and you're biasing towards the null, that's a

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potential problem as well, and inasmuch as in their unadjusted model and their adjusted model, there's increased risk -- there's cause for concern that they may be overadjusting, as I already mentioned, in regards to unshared environment variables.

Q. Unless Dr. Chung is right and this is a genetic disease, right, Dr. Cabrera?

A. There's no data to show that this is strictly a genetically caused disease.

Q. Okay. Did you rely on any other sibling-controlled studies?

A. I did review the previous Gustavson study, the group that preceded this one.

Q. Yeah. It was Brandlistuen. I said it wrong before. Brandlistuen, not --

A. Yes. And I also reviewed Brandlistuen as well.

Q. Okay. And this could not -- on the same dataset, this didn't replicate Brandlistuen on sibling control, right?

A. Well, to be clear, Brandlistuen

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actually looked at different endpoints. And so there were some overlapping endpoints, but they also looked at different endpoints.

Q. Okay. And Gustavson explains why the outcome was different this time, right?

A. They do have some -- they propose some reasons why they may have been different, and one of them was also loss of power because it's based on the discordant siblings that have the particular outcomes.

Q. And the passage of time and the improvement of monitoring and things like that, right?

A. Potentially.

Q. Okay. Even though you criticize sibling control, regulatory authorities recognize it as a -- something that is positive for trying to find a real association versus a non-real association, correct?

A. I don't agree with that. Typically, it's actually the adoption studies that carry the most weight in regards to separating gene environment interactions, not

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sibling-based designs.
Q. Yeah, I didn't say which were the best. I said, you are aware that regulatory bodies recognize sibling-control as superior to not using sibling-controlled, correct?
A. I'm not aware of that.
Q. Okay. And did you find any adoptive studies that evaluated acetaminophen exposure?
A. I did not.
Q. Did you read Dr. Chung's report?
A. I have.
Q. Okay. Did you see her citation to an adoption study?
A. I -- if I did, I hadn't -- didn't notice she had a reference to an adoption study.
Q. Okay. In your work, Doctor, on SSRIs for the plaintiff's Bar, did you encounter what the European regulatory authorities said about the association or lack thereof between SSRIs and autism?
A. I'm not familiar with the

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European statement on that regard.
Q. Okay. Did you ever render an opinion that SSRIs cause autism?
A. I have not.
Q. Okay. Did you ever render an opinion that SSRIs cause ADHD?
A. I have not.
(Cabrera Exhibit 14 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Doctor, I've marked as Exhibit 14 a PRAC document. You may not be familiar with what PRAC is, but it's a risk assessment committee from the European Regulatory Authority.
And do you have that in front of you?
A. Yes, I do.
Q. And I only marked it because they were looking -- and I know you've opined on SSRIs before. They were looking at whether SSRIs can cause autism, and they determined that it -- the evidence does not.
But in the context of a drug exposure and autism, they suggest on page --

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it's 27 of the document on the bottom. It says 27 of 140. They agreed that sibling study design to be the most appropriate to examine such risks in relation to exposure during pregnancy.
And I take it you dis -- you've just testified you disagree with that, right?
A. As I indicated, there is risk for biasing towards a null with those study designs.
Q. Okay. You don't have better data that's better controlled than what we just looked at in Gustavson, correct?
A. Is this a quality assessment? I don't have other sib-paired data in that regard. I think as far as dose effects, we can look at Baker and Ji, and they provide very strong data in regards to those types of interactions.
Q. Right.
But just in a human study like Gustavson, you don't have better control than the sibling control present in Gustavson, right?
If you do, point me to it.

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A. Well, I think the unmatched control in Gustavson itself speaks for itself in regards to that it demonstrates that there's an increased risk. The application of the sib-pair, or particularly the in-family design, as I've already indicated, can bias towards the null, and that's a -- that's a cause for concern.
Q. And your testimony here is that you believe it did bias towards the null, so you do not accept it in your analysis, correct?
A. Oh, I accept it, but I accept it with the understanding that that's one of the risks of doing the sib-pairing design.
Q. Okay. That it is your belief -- Dr. Cabrera believes that a sib-pair design has a risk that it biases towards the null, right?
A. That's correct.
Q. And did Dr. Cabrera do any analysis whether that, in fact, happened in Gustavson?
A. Simply I went over their data analysis and noticed the design that they've

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undertaken and what happened when they applied the model. And so that is a concern with sib-pair design that's understood, generally, as in reference to my report as well.

Q. All right. Did you call on that group at all? Did you contact them in any way?

A. I have not.

Q. Okay. Did you let them know your feelings that what it reflects instead is bias?

A. I wasn't opining about my feelings.

Q. Okay. Well, I mean, if you're genuinely concerned about what you think is causation, wouldn't you go try to tell people, talk to the -- talk to the scientists who found the opposite?

A. If I thought they had an error in the study, then I may reach out to them, if not the editor; more likely the authors first. But it's not that it's an error, I think it's even understood by the people conducting the study that that is a risk.

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Q. Okay. You have no specific facts based on Gustavson to challenge the sibling control. You just have concerns generally about the methodology and bias, right?

A. No. Gustavson, I think, identifies that that's a potential risk in the study itself, and I'm happy to find that for you.

Q. Potential risk, right?

A. Potential risk, yes.

Q. Okay. So how did you -- how did that factor into your analysis, something that powerful? Did you write it off?

A. I wrote up the Gustavson study. It's in my report.

Q. You wrote it up, or you wrote it off?

A. No, I wrote the study up in my report.

Q. Okay. Okay. But then you discredited the findings.

A. I didn't discredit them. I weighed them based on my understanding of that study design and potential limitations

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of it.

Q. And you came to the opposite conclusion of what Gustavson came to in your final analysis, correct?

A. My --

MR. TRACEY: Object to the form.

Robert, read him the conclusion of the authors so we can disaviews {sic} everybody of what they actually said instead of Murdica's version.

MR. MURDICA: Hey, Sean, if you want to testify, I'll put you under oath. But you can't tell the witness where to go and what to do in the middle of an examination whether you're here or not. I'm sorry, but you can't.

MR. TRACEY: Okay. Then I'll object to the form. You're misrepresenting what the authors said. And the easiest way to do this is to look at what they said.

MR. MURDICA: Okay. Thank you, Sean. I appreciate the advice. Send

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me a bill.

QUESTIONS BY MR. MURDICA:

Q. All right. Dr. Cabrera, where publicly have you ever espoused your view that sibling-control design is not a good way to control a study because of the risk of bias?

A. I haven't performed a sib-pair design myself, and so that's not something I needed to voice publicly. But there's literature in that, both in the reference literature and in the published literature, about limitations, and I reference that in my report as well.

Q. Okay.

A. My supplemental report.

Q. You, Dr. Cabrera, haven't published any such thing, correct?

A. Not specifically in that regard, I have not published on that.

Q. All right. Let's talk a little bit about dose.

You, Dr. Cabrera, used FDA guidance to calculate an animal equivalent of a human equivalent dose, correct?

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A. I calculated an animal equivalent dose.
Q. Right.
A. And I also calculated a human equivalent dose.
Q. Right.
And I saw in your rebuttal report that you acknowledged, I believe -- well, let me ask you this.
Do you acknowledge that the guidance that you cited was for calculating an initial safe dose for a first-in-human trial --
A. That --
Q. -- where there's only animal evidence available?
A. That is one application of that calculation.
Q. Well, it's the very title of the document. That's what it says it's for, right?
A. As I indicated, it is the title of the document.
Q. Okay. And you, Dr. Cabrera, then took, even though there's human data,

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you reverse-engineered it back to mouse dose to determine what a safe dose was, right?
A. There's no reverse-engineering. It's simply math. You can multiply or you can divide, and you can then use the scaling between animals and humans to determine whether it's a human equivalent dose or an animal-equivalent dose.
Q. Right.
But in this instance, acetaminophen has been -- we're not doing first-in-human trials, right?
A. It was not a first-in-human trial.
Q. We know what a safe human dose is, right?
A. That's open for debate.
Q. Okay. Well, for 60-plus years, our regulatory authorities have told us what a safe human dose is, right?
A. And they apparently got that wrong, but that's the reason why it's the most frequently caused cases of acute liver failure.
Q. Because the dose is wrong and

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not because it's abused or taken with something else?
A. Because even at clinically recommended dosages, there's been reports of increase in liver enzymes consistent with liver damage.
Q. Dr. Cabrera, regardless of what you think of the approved dose -- and I agree every regulator in the world disagrees with you, and you're entitled to your opinions, but I'm entitled to ask about them.
There is an approved, safe human dose, correct?
A. There is a recommended dose.
Q. Okay. And the guidance that you're using is for when there's not a recommended human dose, correct?
A. The title of that document is in regards to selecting a dose using allometric scaling between an animal and a human.
Q. Okay. So when you already know the human dose, why not -- why are you still using the model for calculating a safe dose for a first-in-human trial?

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A. Because allometric scaling still applies.
Q. Okay. Is this -- is this FDA guidance? Have you used it ever outside the context of litigation?
A. I mean -- just using as an example, this is -- actually, it's not even open for debate. If you look at the label in the Ofirmev, which I've also referenced, and I think we would all agree that at this time, they understood what a recommended dose was. They used the example here in mice of 357 mgs per kg per day, 715 mgs per kgs per day, and 1,430 mgs per kgs per day.
And then they report that as, "These doses are approximately 0.43, 0.87 and 1.7 times the maximum human daily dose respectively based on a body surface area comparison."
That is allometric scaling.
Q. Okay. Did I ask you about that, whatever you're reading?
A. That's exactly what you just asked me about.
Q. Okay. Can I have that folder?

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What else do you have over there?
A. I've already showed you. This is my documents that I've already referenced in my report.
Q. Okay.
A. I gave you the ones that you don't have. And you have that label.
Q. Okay. So this is -- you're referencing a label for acetaminophen that doesn't get processed by the liver?
A. It's a IV acetaminophen.
Q. Right.
A. And part of the utility in that calculation would also include an injection volume, if you wanted to do the calculation that way.
Q. Doctor, you can use whatever tortured method you want. I just got to get a record on it.
So you just showed me an IV application, right?
A. So to be clear, the dosing there is an oral dose that's using allometric scaling.

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The label is for an IV drug. The maximum recommended human dose is based on oral exposure, and the data that they're studying is at animal oral exposure --
Q. I --
A. -- based on a NTP guideline study.
Q. I agree it's based on oral exposure.
IV medication does not first get processed through the small intestine and absorbed into the liver -- absorbed through the small intestine and processed first in the liver, correct?
A. Yes, that is correct.
Q. Okay.
A. That had nothing to do with allometric scaling.
Q. Have -- do you know of -- my original question was whether, outside of the context of litigation, you've used this FDA guidance to calculate either a human dose or an animal dose. And I don't think -- I don't think you answered that.
What's your answer?

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A. Yes. That is -- this is the standard. As it was written into that label, that is what is used.
Q. Okay. When have you used this guidance that we're talking about to calculate a first-in-human dose?
A. Well, not a first-in-human dose. I use the table for allometric scaling. It's literally posted on my wall at work, and we use it to adjust doses. It's based on human exposures to convert them to animal dosages.
Q. Okay. And you don't look at the recommended -- what do you look at, the recommended human dose --
A. Yes.
Q. -- of an approved drug?
A. Yes.
Q. Okay. You've never used it in the way that the guidance is spelled out; in other words, for first-in-human?
A. We use the allometric scaling table, which is consistent with the way it's used in the literature, which is consistent with the way it's used in other labels, if

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you go and you look through the literature.
Even for the acetaminophen label, they're using allometric scaling to determine the maximum human daily dose and then convert that to an animal equivalent dose.
Q. And you saw that all of our -- all of the defense experts criticized your -- the way you calculated the animal dose and said that you're essentially giving them toxic doses, right? You just disagree?
A. Well, they suggested that applying a safety factor would be required for just the allometric scaling, and you don't need an allometric scaling.
The whole idea to find a safe-in-human dose would be if you've already tested in animals and you know the NOAEL, then you could then calculate a human dose, apply tenfold less. That's your tenfold safety factor, and then apply that for first-in-human studies.
That's how that safety factor applies. That's not specific to the allometric scaling, which is based on mixed

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per meter square metabolism differences between humans and animals.
Q. Right.
So you skipped the safety factor part, right?
A. You don't -- you don't -- the safety factor part is part of first-in-human dosing. The allometric scaling is not only used there, but it's also used in EPA guidance in regards to power calculations for converting for animal to human dosage.
It's used throughout the literature. It's used throughout labels. If you pull out any label, you'll see the type of calculation that I did.
Q. Okay. So you just disagree with the defense experts' criticism of the way you calculated that?
A. I think they're misinterpreting.
Q. Okay. Well, you just mentioned EPA. So let's look at EPA guidance -- or not EPA guidance.
AOP 20, which we were talking about before, which your counsel now has a

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copy of, is marked as -- I believe it's marked as Exhibit 1.
If you turn to -- unfortunately, Doctor, these pages are not numbered the way they appear.
So -- well, I have it, but I -- if you're able to turn to Appendix 1. It's a little after that. It's maybe 20 --
A. There's pages at the top.
Q. Okay.
A. Maybe yours is stapled. Under your staple. Under your binder.
Q. Oh, they're on that side.
26, Doctor. Okay. You see it says Appendix 1, and it talks about the MIE and KE and AO, right?
A. Yes.
Q. Okay. The MIEs are listed first, right?
A. Yes, they are.
Q. And that is the binding of essentially glutathione, right?
A. Well, this is sulfhydryl groups, so it doesn't necessarily mean glutathione per se, but it's sulfhydryl

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groups including sulfhydryl groups of proteins involved in the protection against oxidative stress.
Q. Right.
And so it goes from the MIE to the key event to the adverse outcome, right? That's how you get an adverse outcome pathway, fair?
A. Well, each one of the key events is indicated by biological organization, and -- but, yeah, you would -- you would generally follow the key events towards an adverse outcome.
Q. Right.
And the MIE is what you start with, right?
A. In this example, they're described here as molecular-initiating events.
Q. All right. And then molecular-initiating event here is the binding of the thiols by methylmercury chloride, mercury chloride and acrylamide, right?
A. Those are three -- three

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examples of stressors that can initiate these events.
Q. Right.
And it doesn't say acetaminophen is one of the MIEs here to initiate the event with the -- with binding of thiol, right?
A. It's listed as a stressor later in this study.
Q. Not for this MIE, correct?
A. It's not -- it's not under this MIE.
Q. Okay. So if you -- if you now turn to the page with the top 42. Now, this is -- this is the next step in the cascade. This is the key event, right?
A. It's oxidative stress. So it's a key event in this pathway.
Q. Right.
First you have the MIE, right? So the thiols were bound. Now, you have the key event of oxidative stress, right?
A. This is a key event that occurs in the pathway.
Q. Okay. Did I say anything wrong

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in my question?
A. I'm just clarifying.
Q. Okay. And there's three stressors listed here. One is acetaminophen, one is chloroform, and one is furan, right?
A. That's correct.
Q. Okay. And do you know how chloroform works?
A. In what capacity?
Q. As a stressor.
A. I haven't looked into it specifically.
Q. Okay. Did you look at the references underlying this key event in the AOP?
A. Yes, I did.
Q. Okay. And do you remember what it showed?
A. I'd have to look at them specifically.
(Cabrera Exhibit 15 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Let's take a look. This is Exhibit 15.

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Doctor, you now have in front of you Exhibit 15. This, I'll represent to you, and I can show you if you need to, is one of the references for this section of the AOP.
And it's what's specifically referenced for acetaminophen, chloroform and furan as stressors, and you can see it's listed in the references.
Have you seen this before?
A. I believe I did see this reference when I was going through the AOP.
Q. Okay. And do you consider ethanol an oxidative stressor?
A. It can produce oxidative stress.
Q. Okay. And when I asked you before about carbon tetrachloride as an oxidative stressor, do you remember your answer?
A. You had asked me if it was in the pathway. I told you I wasn't sure I had seen that in the pathway previously.
Q. I think you said yes, but regardless, it's not -- it's not listed here,

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right, in -- on page 42 of the pathway?
A. It is not.
Q. But chloroform is?
A. That's correct.
Q. And in your report, you have lots of drawings of molecules, representations of them.
Do you know the difference between chloroform and carbon tetrachloride?
A. Not off the top of my head.
Q. Do you know what chloroform looks like molecularly?
A. I couldn't draw it for you right now if you asked.
Q. Okay. Do you have a chemistry degree?
A. I have a background in chemistry.
Q. Okay. The things in your report that are drawings of molecules, did you copy those from somewhere?
A. If I referenced them, then there would be reference for those studies.
Q. If the pictorial representation is in the report, you didn't draw those,

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right?
A. It's likely I'm referencing in the studies.
Q. Okay. So if I asked you to draw a carbon tetrachloride right now, you couldn't?
A. Carbon tetrachloride I could draw.
Q. Okay.
A. That's a simple compound.
Q. Okay. But chloroform you couldn't?
A. I might not get it right. If this is a -- I don't study chloroforms, so --
Q. Okay.
A. -- how different it is from carbon tetrachloride, I'm not sure.
Q. It's very similar.
A. Okay.
Q. It's only one small difference.
A. And that, I'm not sure about.
Q. Okay. One of the -- one of the chlorines are replaced with hydrogen.
A. Okay. I could draw that.
Q. Yep. Okay.

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So in any event, going back to Exhibit 15, if you turn to the second page which has 64 on the top -- sorry, we're back on this. Sorry.

A. Oh, we're going back.

Q. Did I give you the wrong one? It's Jackson. I believe it's 15.

A. What -- which reference are we?

Q. Jackson.

A. What number?

Q. 15, I believe.

A. 15. Okay.

Q. Flip the page.

A. Yes.

Q. It's the second page.

I'm going to represent to you that this is -- the only mention of acetaminophen in any of the references is right here for why it's included as a stressor.

Do you see in that paragraph it says low-molecular-weight ligands including ethanol, acetaminophen, carbon tetrachloride, chloroform, furan, increase CYP2E's -- CYP2E1's half-life from 7 to 32 hours?

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A. I do see that statement, but it also specifically mentions acetaminophen, particularly in Figure 2, in regards to interactions.

Q. All right. Well, I apologize if I missed that.

Figure 2?

A. Yes.

It's listed as APAP multiple times.

Q. Okay. You're looking at the first and third line?

A. Multiple times. It's listed both under the CYP2E1 ligands based on clustering analysis, if we're looking at risk of cancer generation and inflammation.

Q. Right.

And this is listing the lengthening of the half-life, right? That's what this figure is about?

A. This looks like it's comparing gene expression that results from these exposures that reflect liver cancer, liver regeneration or CYP2E1 ligand interactions and hepatocarcinogens and

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non-hepatocarcinogens.

Q. All right. It's not about oxidative stress, right? It's about the half-life and the hepatocarcinogenicity?

A. Well, to be clear, CYP2E1 is an oxidation pathway, so it is actually about oxidation, yes.

Q. Right.

But nowhere in here does it come to the conclusion that acetaminophen is an oxidative stressor in this article, right?

A. Well, by simply saying it is oxidized by CYP2E1, it becomes an oxidative stressor. It's -- that's -- that pathway is called oxidation.

Q. And you see in this -- in Figure 2 where it's CYP2E1 ligands, it's talking about six-hour half-life, right? That's how it's labeled, 300 milligrams per kilogram, six hours?

A. In that example, there's a 12-hour. There's 24-hour, and then there's also a six-hour, and my --

Q. Oh, you're looking above?

A. -- understanding is there's

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clustering -- that's right.

Q. You're looking above. Okay. Okay.

So you think on the basis of the presence in that figure is why it's listed as a stressor in this adverse outcome pathway?

A. The fact that it's metabolized by CYP2E1 and then consumes glutathione in the production of NAPQI is why it's listed there as being part of an oxidative stressor. Quite literally, that pathway of CYP2E1, it's an oxidation pathway.

Q. But, Doctor, this doesn't say NAPQI anywhere in this article or in this chart, right? That's your -- that's what you were saying, separate and apart from this article, right?

A. CYP2E1 is an oxidation pathway, so being metabolized by CYP2E1, the process is called oxidation. That's why it's part of this pathway.

Q. Yes.

And I just asked you if NAPQI is anywhere in this article.

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A. That -- that's the product of the oxidation of acetaminophen is NAPQI.
Q. And we'll talk about this later, but NAPQI is bound by glutathione if it's produced in the liver, correct?
A. Not entirely, but that is the primary antioxidant that normally would absorb.
Q. And in this -- in this --
A. NAPQI.
Q. In this AOP, the first event was binding the thiols, and then you're stressing it with acetaminophen or some other stressor as listed here, right? So the thiols are already gone?
A. So the -- this stressor as listed is oxidation, and so acetaminophen can produce oxidation, and it produces oxidation through being oxidized by CYP2E1, so it itself becomes a stressor.
Q. In this pathway, the stressor is applied after the first event, which was the heavy metal, correct?
A. If you -- if you wanted to start with a mercury exposure, then

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acetaminophen could be a risk factor in regards to the outcome for heavy metal exposure.
What I've done is shown that acetaminophen is also reducing the amount of glutathione, even at clinical levels in humans, and that that's an oxidative stressor consistent with the AOP 20.
Q. And you've shown that not in your own work, right?
A. I've shown that --
Q. You mean in your report?
A. -- in this report.
Q. Okay. And you saw the -- every defense expert who works on this stuff disagrees with you because they say that there's plenty of glutathione to process the maximum recommended dose with a 90 percent margin of excess glutathione, right?
A. Well, to be clear, we just looked at a study, if you recall, and they had N-acetyl cysteine APAP detected in the cord blood, and so clearly there's not enough glutathione to soak up all of the acetaminophen or the NAPQI.

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Otherwise it wouldn't be in the fetus.
Q. In the cord blood?
A. In the -- in the -- yeah, in the cord blood of the fetus.
Q. Okay. Just because of its mere -- because of its presence, which could have appeared just before the time of sampling, that's your theory?
A. It's not a theory. It's there.
Q. Oh, Doctor, I know -- I believe that you believe all of the opinions that nobody else agrees with in the entire world. I believe you believe them. I'm just trying to get a record.
MR. TRACEY: Objection. Argumentative.
MR. MURDICA: There's not a pending question, Mr. Tracey.
QUESTIONS BY MR. MURDICA:
Q. Okay. So the ultimate part of this pathway is the outcome, and the outcome here is something you attribute to autism, right?
A. It's not just a -- what I

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attribute. It's consistent with the OECD guidelines as I indicated in my report.
Q. Okay. So the outcome of this pathway is, in part, autism according to Dr. Cabrera, correct?
A. The -- no. As the pathway reads, it's an impairment of learning and memory in the AOP, but the AOP also offers guidance in what that means.
And that guidance, which I'll be happy to read into the record, has also been linked to neurodevelopmental diseases and deficits like autism spectrum disorder and postnatal motor coordination deficits.
Q. Okay. So you would link it to autism through this AOP, correct, and you do in your report; is that fair?
A. So those are based on the OECD guidelines.
Q. Do you agree, yes or no? You would link this -- you would link this AOP to autism, and you do in your report, correct?
A. Consistent with the OECD guidelines, I would say that impairments in learning and in memory in children and animal

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models and regarding the oxidative stress that caused neurodevelopment disorders, the AOP indicates oxidative stress, and I'll quote, "Has also been linked to neurodevelopmental diseases and deficits like autism spectrum disorder and postnatal coordination motor deficits."

Q. And you rely on this AOP for your causation opinion on autism, right?

A. So I apply that AOP to see if there's any gaps in the mechanism for understanding whether there's a biological plausibility.

Q. Right.

And the outcome here is learning disability, right?

A. Impairment of learning and memory.

Q. Impairment of learning and memory.

And you use this outcome and extrapolate it to autism and ADHD, correct?

A. So to be clear, it's not just my extrapolation. It's consistent with OECD guidelines on what have also been linked

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with these -- with these outcomes.

Q. I understand that.

But you also -- you you can read what you read, but you also -- Dr. Cabrera extrapolates it to autism as well in your report, right?

A. I -- the testing that is used, some of those also measure the same developmental neurotoxicity guideline testing that are also -- that are also included in autism core behaviors and in animals as well.

Q. Right.

So you took all of that, and you extrapolated this AOP to autism for your causation opinion, right?

A. I used it to see if there was -- to identify whether there was deficits in the mechanistic cascade as part of biological plausibility for my causality analysis.

Q. And you found this compelling for your causality analysis for autism, correct?

A. I found that there weren't gaps in the data in regards to a biological

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plausibility.

Q. Okay. Are you -- is there some reason you can't give a direct answer to my question? Do you find this compelling for autism as an outcome in this pathway or not?

A. As indicated, these -- and I'm happy to, you know, speak specifically to that. The testing in the animals, they produce core behaviors that are consistent with what we refer to as autism core behaviors in the animal. So that's part of the animal impacts.

Those parallel to human. And so there is a parallel there. I'm not extrapolating. It's just a parallel.

Q. Okay. And that parallel is why you used AOP 20 for your causation opinion as to autism, right, among other things?

A. Among other things.

MR. MURDICA: Okay. Let's mark this as 16.

(Cabrera Exhibit 16 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Doctor, did you know that this

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was -- that AOP 20 was rejected with respect to autism before its publication?

A. I have not seen this --

Q. Okay. So --

A. -- internal review.

Q. So this is new to you; that they specifically rejected connecting it to autism?

A. I haven't seen this document that you've just given me.

Q. Okay. Do you want to take some time to look at it? Because I'll represent to you that AOP 20 originally had an outcome of autism, and it was rejected for lack of validity.

MS. KING: Do you have a copy?

MR. MURDICA: I don't. I only have my copy.

THE WITNESS: Do you want to go off the record? We can make copies and --

MR. TRACEY: Yeah, make a copy of it and read it, Robert. And somebody send me a copy.

MS. JOHNSTON: No problem.

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Let's go off the record and handle that.

VIDEOGRAPHER: Off the record, 3:40.

(Off the record at 3:40 p.m.)

VIDEOGRAPHER: The time is 3:56 p.m., back on the record. Beginning of Media 6.

QUESTIONS BY MR. MURDICA:

Q. Dr. Cabrera, are you ready to proceed?

A. Yes, I am.

Q. Okay. Welcome back.

Dr. Cabrera, what's in front of you is marked Exhibit 16, and before we get into it, I have some questions for you. You -- we've talked a lot about AOPs today.

Have you ever been part of an AOP review?

A. I have not.

Q. Okay. Have you ever submitted an AOP yourself for review?

A. I have not.

Q. Okay. Is the -- are you familiar with the review process that AOPs go through?

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A. Yes, I am.

Q. Okay. Is it from reading this document, or did you know beforehand?

A. I actually -- there was a presentation on it this year at Birth Defects Research Prevention, and I had lunch with the person that had just submitted an AOP, so we talked about it extensively.

Q. So in other words, you were at a conference and somebody -- another attendee explained to you the process because they were going through it?

A. Well, I was already familiar with it, but then he also gave me a firsthand account.

Q. Okay. And you see on the first page of Exhibit 16, there are reviewers, right?

A. Yes.

Q. And there's a primary reviewer and two secondary reviewers, correct?

A. That's what I see, yes.

Q. Okay. And the first one has an e-mail extension of @canada.ca.

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Do you know if that's someone in the Canadian government?

A. It looks like they might be, that canada.ca, or is that -- yes.

Q. It may -- it may be governmental, right, Doctor?

A. Maybe.

Q. Okay. And the secondary reviewer, number 1, is someone who appears to be from some regulatory body in the Netherlands potentially?

A. I'm not sure what rivm is related to.

Q. Okay. But the third reviewer, the secondary reviewer, number 2, you know where that person is from, right?

A. Yes.

Q. And where is that?

A. Their domain is epa.gov.

Q. Okay. And I take it you've had a chance to review this document now --

A. Yes, I have.

Q. -- on the break?

Okay. And you understand it to be the review of AOP 20, correct?

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A. I do.

Q. And this was a prepublication review, right?

A. Yes.

Q. Okay. And one of the things we see is that AOP 20 had been copied from another AOP, correct? Based on your review, does that -- what it appears to have been?

A. It sounds like it was modified from an existing one.

Q. Right.

It was essentially copied, pasted and then modified, right, with a different MIE?

A. Potentially. I didn't get the specifics of that in my reading, but it sounded like at least part of it was used in this AOP.

Q. And one of the -- and you correct me where I'm wrong here, but I'm just trying to make it easier so we can get through it.

One of the main points of feedback from all reviewers is that the outcome in this pathway that's explained

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should not be autism, correct?
A. I think the, you know -- my reading, we can do particular quotes if you want, but my reading of it is that if it's going to be autism, they need to state that it's autism. If it's going to be as endpoints in impairment to learning and memory, then they need to make it impairment to learning and memory, to pick one.
Q. And they need to have the data to back it up if they're going to keep autism in, correct?
A. Yeah, there was some conversation in regards to what it would mean -- what changes would be required if it was autism as opposed to learning and memory.
Q. And, in fact, the author's response was, quote, "We can totally remove the autism aspect and consider only learning and memory impairment, for which there is enough experimental support."
Correct? Do you see that?
A. If you're doing a quote, I'm not sure what page you're on.
Q. I wish I could tell you.

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They're not numbered. I can show you my copy. It's right there.
So my question is, the author of AOP 20 in response to the feedback on removing autism from the three reviewers said, quote, "We can totally remove the autism aspect and consider only learning and impairment for which there is enough experimental support."
Did I read that correctly?
A. That is a correct reading.
Q. Okay. Did you know before we sat here today that AOP 20 didn't have enough experimental support to include autism as an outcome?
A. I hadn't seen this study prior to you showing this internal review. I hadn't seen this internal review.
Q. Okay. All right. We can put that aside.
In your report, you have numerous potential proposed pathways?
MS. KING: I'm sorry, I just got that text. So I'm taking over now, if that's okay. Just letting you

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know.
MR. MURDICA: Okay. You're defending the deposition in person?
MS. KING: Yes.
MR. MURDICA: Okay. Is Sean okay?
MS. KING: It's okay. It's okay. I'm sorry to interrupt. I just wanted to -- everybody to know if I start talking, that's why.
MR. MURDICA: Okay. All right. We can take a break at any time if necessary, and we're all fine with that.
MS. KING: It's okay. I'm good.
QUESTIONS BY MR. MURDICA:
Q. Okay. I believe you would put them all in the categories of biologic plausibility, but you proposed several mechanisms, I would say, by which acetaminophen could affect neurologic outcomes in your report, right?
Let me give you some examples.
You proposed that

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acetaminophen, as we just talked about with the AOP, could cause oxidative stress via depletion of glutathione and generation of excess NAPQI that the glutathione can't process, right?
A. I've seen in studies that acetaminophen can lower glutathione levels and cause oxidative stress.
Q. Right.
And then your theory goes that the oxidative stress can happen not just in the liver, it can happen in the fetal brain, and that stress -- right -- am I with you so far?
A. I'm following you.
Q. Yep. And you say that, right? The oxidative stress can happen in the fetal brain, right?
A. Yes.
Q. Okay. And then the outcome of that from oxidative stress in the fetal brain is some sort of neurological damage, right?
A. Well, it influences the behavior of cells by changing the oxidation in the -- in the cells.

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Q. Right.
And the effect on the cells in your theory would be the exact right way to induce ADHD or autism, right?
A. You --
(Discussion held off the record.)
QUESTIONS BY MR. MURDICA:
Q. I can do that again, if you'd like.
A. Please.
Q. Okay. That the proposed oxidative stress in the fetal brain can cause some sort of neurologic damage that's the exact type of cellular damage necessary to create the presentation of ADHD or autism, correct?
A. So there's a lot there in that interaction inasmuch as changing the redox -- the redox potential of cells changes their behavior. So it can influence the behavior of cells during the developing nervous system, and that can produce adverse outcomes specific with increased risk of autism -- autistic core behaviors.

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Q. Right.
And in the section of your report that discusses that mechanism, most of the endpoints are just neurologic toxicity, not autism and ADHD themselves, correct?
A. Well, it works through there sequentially. So at a molecular level, you don't see autism or autistic core behaviors neither at a cellular or a tissue level, per se. You would only see those at an organism level.
Q. Right.
But the pathway that I just described is your -- it's your oxidative stress proposed pathway to get from ingestion of acetaminophen to autism in a human baby, right?
A. That is one application, yes.
Q. Right.
Now, you included, I think, five or six other potential pathways in your report as well, right?
A. I reference interactions, things that happen in parallel with that.
Q. Yeah. Antagonism of the

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endocannabinoid pathway, right? That's one?
A. I did mention, yes, endocannabinoids.
Q. Okay. You gave me a paper today that talks about notch signalling and SOX2, right?
A. That's correct.
Q. Are you adding that as a proposed mechanism?
A. Not currently, other than the fact that they did acetaminophen exposure and they're looking at particular changes in that signalling pathway. So that's a proposed signalling pathway for impacts on the hippocampus, but I'm not -- I haven't started drafting anything about that as a pathway.
Q. Right.
And I'm just asking you today, regardless of whether you started drafting something, are you -- are you going to propose that as a biologically plausible pathway based on the -- on the Xie article that you handed me today?
A. In and of itself, there is some other hippocampal data and impacts, but I --

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that's not something I currently plan to do.
Q. Okay. Ultimately, when you came to your causation conclusion in this case, which pathway -- because you proposed many others, which pathway did you pick?
A. So the two that I found evidence for when applying the AOP model was the oxidative stress and the endocannabinoid pathways.
Q. Okay. And the rest of them you included as background, essentially?
A. Well, just in regards to there are other things that happen -- biological systems that can interact with those pathways, but those are the core pathways.
Q. Right.
The other ones outside of the endocannabinoid and the oxidative stress you agree are not -- they either don't make it all the way along the pathway or they're not specific to autism or ADHD, correct?
A. So specifically applying the AOP, there would be gaps in the data that would leave a gap in the biological plausibility that would need additional data

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to fill in those gaps.
Q. So Dr. Cabrera, for his causation opinion, is going on oxidative stress and endocannabinoid antagonism, right, as pathways?
A. Well, I don't know about antagonism inasmuch as increasing agonist signal through an anandamide would also be -- would also be an interaction. So not strictly just antagonism because there's also some agonism going on there.
Q. But that's still an -- the endocannabinoid pathway?
A. It's still the endocannabinoid pathway.
Q. Okay. And now that you've seen that AOP 20 was not intended to be used for the outcome of autism, are you going to stand by your opinions here?
A. So I use the same methodology as described in -- as I had already mentioned, the same methodology that was described in AOP, to come to the similar adverse events, which include impairment of learning and memory, which overlap with core

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autism behaviors.
Q. Right.
Some autistic patients have impairment of learning as a symptom. Some, but not all, correct?
A. That is correct.
Q. Okay. So you're going to rely on a pathway that leads to a symptom for some autistic patients to apply to ADHD and autism for all patients, correct?
A. Not for all patients. It would have to be -- I mean, if we're talking about case-specific, you have to consider both genetic and environment interactions. This is simply looking at the biological plausibility of those interactions.
Q. Right.
So according to Dr. Cabrera on the AOP 20 pathway, it's biologically plausible to get to impaired learning, correct?
A. So using the AOP 20 as a framework, we can move from -- and I can walk through that.
Acetaminophen can reduce

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glutathione and that can increase risk for oxidative stress. It's been shown in humans, even in regards to modeling in pregnant mothers. There's NAPQI there.
And you can look at that effect. In particular, if you want to look at embryos or fetuses, you have to look at animal models. But we've seen that there's changes in glutathione in the animal models, the presence of acetaminophen in those animal models, and we've seen the adverse events that are produced in those animal models. And those parallel what we see in the literature in regards to epidemiological studies.
So that's a totality of data there when we -- when we apply this model to those experiments.
Q. Right.
And the impaired learning that you get to from AOP 20, because it's a symptom of one of your two outcomes, because it's a symptom of autism, you're extrapolating it to the -- to the entire autism population as a possible causal factor

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and to ADHD, correct?
A. Well, it's not just impairment in learning because we also see some other autistic core behaviors in the animals that are exposed to acetaminophen.
Q. Okay. And your theory, without human evidence for legal and ethical reasons, is that acetaminophen can make it across the fetal blood-brain barrier in enough quantity to deplete all the glutathione in the fetal brain and generate enough NAPQI in the fetal brain to cause oxidative stress and cause neurologic changes during development, correct?
A. It doesn't need to be a complete depletion of glutathione. So that's not correct.
Q. Okay. Anything else about what I just said wrong? Is there anything else wrong with what I just said?
A. Well, just to clarify, it doesn't need to be a complete depletion of glutathione.
Q. Is glutathione not -- in the opinion of Dr. Cabrera, not effective at

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finding NAPQI?
A. It is, but it doesn't need to be a complete depletion in order to change the cell behavior of stem cells or neuro stem cells.
Q. Is it your testimony that NAPQI that's bound with glutathione -- to glutathione can still change stem cells?
A. Changing the reduction potential in a stem cell population will change the behavior of the cells as indicated in my report.
Q. Okay. Even if -- does that apply, according to Dr. Cabrera, even if only 10 percent of the glutathione is needed to bind all of the present NAPQI?
A. As has been shown, the -- that's not a true statement because there's already N-acetyl cysteine bound to glutathione found in the cord blood. So it's not enough in order to bind all of it.
So some of it is getting to the fetus, and some of it is being metabolized by glutathione in the fetal compartment.
Q. So now you're relying today,

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Dr. Cabrera, on the 118 patients in the 2020 Ji study that had acetyl cysteine metabolite in their cord blood to substantiate your theory?
A. That also supports the biological plausibility and the causality. It's in totality. You can look at the breadth and the depth of the data, and it supports this interaction and this causality.
Q. I believe that you believe that, Dr. Cabrera. I do. I can tell you're earnest.
All right. Let's take a look at -- one of the things I think you said you looked at, Dr. Cabrera, is the documents produced about FDA's own analysis of this, right?
A. Yes.
Q. I take it you didn't bring it with you?
A. I did not.
(Cabrera Exhibit 17 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Cabrera, you should

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now have in front of you what's been marked as Exhibit 17.
Do you have that?
A. Yes, I do.
Q. All right. And these are documents that you reviewed before, right?
A. I've seen them.
Q. They're on -- they're in your reliance materials?
A. I believe they are, yes.
Q. Okay. And they're -- you can tell from the appearance of the first page, can you not, that these are documents authored by the United States Food and Drug Administration?
A. Yes.
Q. Okay. Doctor, you have never been asked by FDA to weigh in on a drug label, have you?
A. I'm not a labeling expert.
Q. Okay.
A. I've not been asked.
Q. Okay. In your report and at your deposition today, you've offered opinions about what warnings or what labeling

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is present on acetaminophen.
Do you remember saying that?
A. I don't know about specifically, but we did have a conversation about that.
Q. Let me -- let me -- let me ask you a question.
Are you intending to offer an opinion on what the acetaminophen packaging or labeling should say?
A. I'm not.
Q. Okay. So the section in your report criticizing the labeling, should that even be in there?
A. I didn't -- I didn't know that I had a specific criticism of the label. I would need to see the specific reference you're referring to.
Q. Okay. In any event, is it accurate that you're not here today to offer any opinion, expert or otherwise, as to what the label should or should not say with respect to pregnancy with respect to acetaminophen?
A. I mean, I have an opinion on

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it, but I'm not a labeling expert, so I wouldn't be offering my expert opinion on that.

Q. Okay. And you do know, though, what the FDA to date has said about whether or not the label should say anything about the risk of autism or ASD or any neurologic defect during pregnancy with the use of acetaminophen, right?

A. I'm aware that they're planning on continuing studying this matter and that it's still open for debate.

Q. And that they have been looking at it for -- since at least 2014, right?

A. At least since 2015, in their report, so I assume it started somewhere before then.

Q. Uh-huh.

And even though they're looking at it, they've had opportunities for -- you know, since that period of time to come out and say that the label should be changed, and that has never happened.

They've stuck by the advice that women should contact their physicians

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before taking any medication, right?

MS. KING: Objection. Form.

THE WITNESS: I think that's good advice. That being said, unfortunately, even in the absence of evidence, it has been widely assumed to be safe during pregnancy.

QUESTIONS BY MR. MURDICA:

Q. Right.

And it's up to the physician to advise if a patient follows the current labeling and calls a physician, it's up to the physician to offer his or her recommendation on whether, for that particular patient in that particular circumstance, acetaminophen is an appropriate treatment, correct?

MS. KING: Objection. Form.

THE WITNESS: If it says to contact your physician during pregnancy, and the physician could make that opinion, but I guess the concern is whether they're fully informed on making that opinion.

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QUESTIONS BY MR. MURDICA:

Q. Right.

And you don't know one way or the other because you don't know what every physician in the country knows or believes or thinks, right?

A. I do not know what every physician in the country knows or believes or thinks.

Q. And even though you don't prescribe medicine, it's a risk-benefit analysis no matter what, right?

A. I'm familiar with risk-benefit analysis and, yes, that would apply here.

Q. You know there are women with epilepsy who stay on antiepileptic medications during pregnancy, despite known risk of birth defects with the medication they may be taking, right?

A. I'm aware of that.

Q. And you don't doubt that that's a better gamble than the woman and the child dying if, for example, in a motor vehicle accident due to an epileptic seizure, right?

MS. KING: Objection to form.

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THE WITNESS: To be clear, the -- I -- I've spoken about this with treating physicians, and they've indicated they would normally switch to medications that have not been -- such as away from valproic acid, to switch to medications that have not been associated with adverse outcomes.

And then try to stabilize the epilepsy prior to pregnancy would be the preferable route.

QUESTIONS BY MR. MURDICA:

Q. Yeah. If they can, but that's not always a possibility. You know that, right?

A. I'm aware of that.

Q. Okay. Back to Exhibit 17, if you turn to Bates label 158. So you've never looked at FDA's internal regulatory documents before, I take it, unless it was in the context of litigation?

A. In the context of litigation, I have.

Q. Okay. And I know you're not going to offer a labeling opinion, but did

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you see in your review that revising a label was something FDA put a red X on when they reviewed the data that we're going to -- the pregnancy data we're going to review here?

Had you seen this before today?

MS. KING: Objection. Form.

THE WITNESS: So my read of this document was there was some questions raised in regards to reviewing the label, but I do see the red X that you've indicated on the page.

MR. WATTS: What's the exhibit number?

MR. MURDICA: It's 17.

QUESTIONS BY MR. MURDICA:

Q. Okay. Do you recall reading -- you know FDA did their own epidemiologic analysis with their own science -- scientists at various points in '14, '15, '18, '20 and '22, right?

MS. KING: Objection. Form.

THE WITNESS: I -- I'm aware that they've had ongoing analysis. I have to look specifically in regards

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to the years that you've mentioned.

QUESTIONS BY MR. MURDICA:

Q. Okay. Without reference to the years, did you see that they review many of the human studies that you reviewed in your report?

A. They've reviewed some of them, not all of them.

Q. Okay. Yeah, I said many.

So it depends on when you look, right? The most recent review that we have, I believe, is in 2022, so it would be missing whatever came out in the rest of '22 and '23.

Is that what you're referring to?

A. In part, yes.

Q. Okay. Did you compare your review of the studies to FDA's review of the studies before you finalized your report?

A. I was already familiar with the FDA's review of the studies, the past.

Q. Okay. You know FDA review -- reviewed animal studies about in utero acetaminophen exposure, right?

A. I did see some of that as well,

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yes.

Q. And did you see -- and that's called nonclinical review, right?

A. Well, we generally refer to it as preclinical.

Q. Preclinical?

In their pre -- their preclinical reviewers came to a conclusion that additional animal data was not likely to be informative.

Did you see that?

MS. KING: Objection. Form.

THE WITNESS: I read some correspondence where the findings were of concern, but in regards to conclusions, there was, to me, some mixed signals. In the epidemiology, they needed some more mechanism data which can be found in the animal models.

And in the animal models, they wanted more specific information on outcomes, which is found in the human studies. So you really need to look at those together.

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QUESTIONS BY MR. MURDICA:

Q. Dr. Cabrera, the preclinical reviewers, what they were really saying is that the outcomes in animal models aren't close enough, predictive enough to ASD and ADHD in humans for further studies to elucidate the issue, right?

MS. KING: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. Whether you agree with it or not, that's what they -- you know that's what they said, right?

MS. KING: Objection. Form.

THE WITNESS: Well, if you want to find a particular quote, we can -- we can look at that, but...

QUESTIONS BY MR. MURDICA:

Q. Okay. I'm just asking -- let me ask it this way.

Do you remember them -- do you remember that being their rationale for saying that additional animal studies are not likely to be informative?

A. For their rationale behind that?

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Q. Yeah.
A. The applicability, as I mentioned, because these are animal models, whether that was informative on a human outcome.
Q. Right.
Because animal outcomes like we were talking about earlier, where you're looking at marbles and socialization and everything, the FDA reviewer didn't see those as being relevant enough to human symptoms in autism and ADHD, correct?
MS. KING: Objection. Form.
THE WITNESS: I can't say. You know, I can't read the person's mind, per se, but the -- my takeaway from this information was that there were some reservations in regards to the utility of the animal data for application in the clinical outcomes.
The clinical outcomes claim the same deficiency, that they needed more mechanistic data, which is provided with the animal studies, which really you have to look at that data in total

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to understand what's going on.
QUESTIONS BY MR. MURDICA:
Q. And, Dr. Cabrera, that -- as somebody who works on animals every day, that must have jumped out to you, that they didn't think any additional animal data would be -- would provide more information, right?
A. It's -- it's not the first time I've heard something like that.
Q. I take it you disagree since you work on animals.
Is that fair?
A. That's a -- I think that's partially correct inasmuch as we do develop animal models of human disease. We do appreciate, as I've already mentioned, there's differences in species, and that those are models of human disease.
And I think that inasmuch as we can do experiments on them that we couldn't do on humans, they serve their purpose in that regard.
Q. All right. If it -- I take it -- I may have asked you this before. You haven't attempted to tell FDA that you think

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you've got the animal model better than they do, right?
A. I haven't done my own acetaminophen studies in my laboratory.
Q. Okay. So you just review the existing studies differently than the FDA reviewers do, right?
MS. KING: Objection. Form.
THE WITNESS: I don't -- I don't know that I review them differently inasmuch as I just performed a systematic review, but I'm considering the totality of data, not just siloed data.
QUESTIONS BY MR. MURDICA:
Q. Okay. In other words, you don't know what FDA reviewed or didn't review; is that what you're saying?
A. Not in total.
Q. Okay. So if you were to -- I know you haven't done any studies on acetaminophen.
If you were to do one, what would you do in your lab or -- well, you can't do one in your lab. If you were to do

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one in a lab, what would you do?
A. Are you just asking me to design an acetaminophen study?
Q. Yeah.
Have you thought about it?
A. I have.
Q. Okay. And what would you do?
A. So our normal study design, we would -- we would actually follow guidelines. We do guideline studies predominantly in my laboratory, so we would follow study guidelines in regard to animal models and the number of animals required.
We would do exposures. Our exposures, we would include a dose-response in regards to exposures, typically at the minimum, two-dose, but typically three dosages.
And we would determine changes in maternal weight to make sure there's not maternal toxicity per se, and then we would look at the weight of the dam throughout pregnancy. We would look at the weight of the pups when they're born.
And then we would divide them

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up beforehand blindly between what their exposure was or non-exposure into different testing groups, and those would go then downstairs into the behavioral testing facility for analysis.

Q. And you would give them the same behavioral tests that we talked about earlier, the three-chamber test, for example?

A. That is one test that we could run, yes.

Q. Okay. You don't have any additional or special tests compared to what's in the literature?

A. I don't know about special. A lot of -- our strength is that it's -- our system has largely been automated, so we can do tracking that doesn't require an attendant. You can review the data, but it's largely automated to remove any potential bias.

So you're blinded to the treatment of the animals and the groups, and the machines do the -- do the data collection.

Q. And the data you collect in

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your hypothetical study would only be as good as the model is in terms of measuring those behaviors that you associate to human autism and ADHD outcomes, correct?

MS. KING: Objection. Form.

THE WITNESS: If -- I mean, in turn, the model is as good as the model can be, and as a potential comparison, we could do a valproic acid exposure as a -- as a control in addition to treatment with acetaminophen.

QUESTIONS BY MR. MURDICA:

Q. But even valproic acid doesn't induce autism or ADHD in every exposure, right?

A. It produces autism core behaviors in a majority of animals, but not in every animal.

Q. If you turn to 147, which is like the third page in on this, and you look at the second paragraph down.

Now, this is -- this is talking about 2016.

Do you see where it says

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"nonclinical data"?

A. Can you give me the Bates number on that?

Q. Sure. It's 147 at the bottom. The top of the page, second paragraph.

A. Okay.

Q. So, Dr. Cabrera, you know, because we talked about it earlier and you volunteered, that around this time, FDA came out with a statement about ADHD and acetaminophen, right?

A. Could you repeat the question?

Q. FDA issued a statement -- a guidance online about ADHD and acetaminophen and said they would continue to monitor the data, but essentially recommendations on use haven't changed?

A. I'm familiar with that statement.

Q. Okay. And you see here the conclusions that led to it internally, right? Oh, sorry.

A. I see specifically the paragraph, their comments in regards to the animal studies.

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Q. Right.

Okay. And this is what I was -- this is what I relayed to you before, right, that behavioral responses in animals that are most likely predictive of an ADHD response in humans are uncertain and, therefore, additional animal studies are not likely to be informative.

That was their view, right?

A. That is a quote in this document.

Q. Okay. And then the next paragraph on March 1st of 2016, whoever was doing this review at FDA agreed, the data did not support a causal association between acetaminophen and ADHD at the time, and the TSI would be closed?

A. I see that as well.

Q. Yeah.

And you know you disagree with that today, but you don't know if you would have disagreed with that in 2016, right?

A. I do not know.

Q. Okay. All right. And then if you look down at the bottom of the page,

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there was also human data reviewed, and this was later. This was a year later.

And the reviewers said, "Although we have more studies, we do not have higher quality data to better inform drug causality, and with these findings being in clinical practice, all of these studies had significant limitations, uncertainty and critical missing information that precludes reliable inference of drug attribution."

Do you see that?

A. So I -- just to be fair, the statement begins with "We acknowledge the consistency of findings of positive association between APAP and adverse neurodevelopmental outcomes in the majority of published observational studies reviewed to date."

And then it follows, "Although we have more studies, we do not have higher quality data to better inform drug causality and what these findings mean in clinical studies. All of these studied has significant limitations, uncertainties and critical missing information that precede --

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preclude reliable inference of drug attribution."

Q. Right.

And you're familiar with the ADHD studies that existed as of February 2017, right?

A. I've reviewed them.

Q. Yeah.

And we haven't gone through all of them, and it would -- it would take a while to do so, and we're not going to do that today.

But you know that many of them were -- they were data collected essentially by surveys, right?

A. Several of them were survey data.

Q. Yeah.

And they relied on maternal memory sometimes years after the pregnancy, right?

A. I -- I'm not going to comment generally on how close temporality -- temporally they were to when they collected the data, but several of the studies did use

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questionnaires in order to collect the data based on maternal recall.

And just to reiterate, generally maternal recall would bias towards the null, not away from.

Q. Well, that's -- I understand you're saying that generally, but in the case of surveying for mothers for children with neurodevelopmental issues, you know it's the opposite, right? The -- there is a bias for responders for children that actually have the condition, right?

A. Well, if -- that would assume that they were developing a bias based on they're not sure what they're supposed to be recalling in regards to that bias.

Q. Well, did you see, Dr. Cabrera, that in some of the studies -- some of the surveys, the questionnaires, large percentages of the respondents were lost to follow-up over the years because some of these went to, you know, age 7 of the children, right?

A. That does happen.

Q. Right.

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And it happened in the studies. You saw that, right?

A. It does happen.

Q. Yeah.

And the people who were still responding at year 7 are biased towards mothers who are concerned about their children that actually have problems, right?

MS. KING: Objection. Form.

THE WITNESS: I don't know that that's a bias in that regard, but there may be -- and I'd have to look specifically at that, whether that was -- there was a correlation between having an affected child and not being lost to follow-up.

MR. MURDICA: Okay. Why don't we take a break at this point. I need about five minutes, just figure out what the last bit we're going to do is.

Does that work for you, Doctor?

THE WITNESS: I can do that.

VIDEOGRAPHER: Off the record, 4:36.

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(Off the record at 4:36 p.m.)
VIDEOGRAPHER: The time is 4:56 p.m., back on the record. The beginning of Media 7.
QUESTIONS BY MR. MURDICA:
Q. All right. Dr. Cabrera, are you ready to proceed?
A. Yes, I am.
Q. Okay. Doctor, we're going to talk about some things that Dr. Cabrera believes acetaminophen can and cannot cause. Okay?
Can acetaminophen, in the opinion of Dr. Cabrera, cause neural tube defects?
A. Only at doses that wouldn't -- that would be outside the normal intake.
Q. Okay. So I'm -- that's a good point. I'm going to limit my questions to therapeutic -- normal therapeutic doses in line with the labeling.
For a normal therapeutic dose, does Dr. Cabrera believe that acetaminophen causes major congenital malformations in human beings?

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A. I've only seen one study that would support that in regards to the National Birth Defects Prevention Study, and that wouldn't be enough data to draw that conclusion.
Q. Okay. Does Dr. Cabrera believe that acetaminophen at a therapeutic dose can cause trisomy in an offspring?
A. I haven't seen any data that would support that it would cause a trisomy.
Q. Okay. Does Dr. Cabrera believe that acetaminophen at a therapeutic dose in any human, not just during pregnancy, can cause hard cancers?
A. Solid tumors, is that --
Q. Solid tumors.
A. I've only seen data, as I've indicated in my report, consistent with leukemias, not solid tumors.
Q. Okay. So the answer on solid tumors would be no, right?
A. Correct.
Q. Has Dr. Cabrera seen enough data to say that acetaminophen at therapeutic doses can cause and does cause leukemia in

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patients taking acetaminophen?
A. I've seen data that supports that. I haven't done a causality analysis in that regard, but I would say there's data that's consistent with causality. But I haven't performed a causality analysis for that.
Q. Okay. And the data that you've seen that you say is consistent with causality relies on induced de novo mutations, essentially, from acetaminophen as a pathway, correct?
A. It's oxidative damage that can increase the risk of de novo mutations.
Q. Right.
And --
A. And chromosome breaks.
Q. -- and Dr. Cabrera knows that if that was true, you'd also see solid tumors as well as blood cancers, correct?
A. Not necessarily, as solid tumors weren't found in the animal models, nor have I seen reports in humans for solid tumors in that regard.
Q. Okay.

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A. And I'll add that it, oftentimes, particularly may affect highly proliferative cells. And that may be why it's leukemias as opposed to other solid tumors.
Q. In any event, as of today, Dr. Cabrera hasn't seen enough to say and put out for the world that you believe acetaminophen in therapeutic doses causes blood cancers, do you?
A. I haven't conducted a causality analysis on that, so I would not be willing to make that opinion.
Q. Okay. What confounders should we be accounting for in assessing causality between acetaminophen exposure and the pregnancy outcomes of discussion ASD and ADHD?
A. So to be clear, our animal models remove those confounders. That's one of the strengths of them. And so we don't have to worry about environmental or genetic confounders in our animal models. But I can also speak specifically in regards to human studies as well, if you'd like.

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Q. Yeah, let's talk about human studies.

What confounders should be taken into account?

A. So some of the things that have also been determined as risk factors, and we've talked about earlier, so potentially smoking or the use of other medications. And that would include things like valproic acid, exposures to heavy metals, whether those are environmental or occupational exposures.

And as a more general statement, you need to consider -- those are just known risk factors in that regard. You need to consider all the various factors in order to do a weighted analysis for that.

Q. How about maternal or paternal ADHD?

A. You have to consider this as a potential risk in that there may be some genetic liability as well if there's maternal or paternal ADHD or ASD, even, for that matter, present on the mother or father. It's a potential genetic component.

Q. Particularly if the offspring

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ends up with ADHD and the parents or parent have ADHD, even Dr. Cabrera would be suspicious of a genetic cause there, right?

A. I don't know about "even Dr. Cabrera," but actually one of the first things we do is normally conduct a genetic analysis.

Q. Okay. Because you would be suspicious for genetics as a cause there, right?

A. Well, it's because it's one of the tools we have in the laboratory. We like to apply the tool to see if there is a genetic cause. It's --

Q. Right.

A. -- an open question that we normally apply upfront.

Q. And if the parents have the condition, you're not doing it for laughs; you're doing it because you suspect that's a possibility, right?

A. Yeah, we do -- typically we do a trio analysis, and we'll look for rare variance or mutations in the mother or father, or look for de novo mutations as

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well. So you could have two rare mutations come together in the offspring and that could increase disease risk, or you could have de novo mutations that could also increase disease risk as potential genetic factors.

Q. Okay. Back to confounding in human data that Dr. Cabrera believes we need to account for here.

Is impulsivity in the mother a risk factor?

A. I haven't seen specifically impulsivity as a -- as a risk factor for autism.

Q. How about anxiety?

A. I think there's some overlap in regards to anxiety and autism or ADHD behaviors, and so there -- that could be a facet of the presentation that should be considered.

Q. Okay. So anxiety in the mother is something you would consider as potential confounding?

A. Something in -- as reviewed -- if you think about this as a part of the nurturing environment, then you have the

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potential for mom and dad to not just provide genetics in regards to the offspring, but also how they influence the environment; both the in utero environment and also the environment that the child would be exposed to, you know, afterwards.

Q. Have you seen data on whether anxiety in a mother increases the risk of ADHD or autism in the child?

A. I've seen analysis on various behavioral interactions. I'd have to look back specifically for anxiety.

Q. Okay. Would Dr. Cabrera today consider that confounding for the outcome of interest or potentially confounding or not?

A. I think potentially it should be considered if it -- particularly if it's severe or debilitating.

Q. And if I asked you that same series of questions for depression in the mother, would I get the same answer?

A. Well, actually, slightly different answers. And the question is whether the depression is being treated and with what other medications it could

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potentially being treated with, and you'd have to be concerned about potential exposures to those medications as well.

Q. Okay. How about untreated depression, potentially confounding or no?

A. It depends on the severity and whether it's -- has -- oftentimes, I'm sure you're aware, there can be risk behaviors associated with depression. And so you would need to account for that if there's particular risks associated with that depression.

Q. Okay. Any other confounders you can think of other than the ones we discussed?

A. So generally what is also often adjusted for is -- drinking or smoking is also usually adjusted for in those models as well.

Q. One quick question, and this was just something I wasn't sure.

In your report you have a biological gradient section, right?

A. Okay.

Q. And it says, "Meta-regression

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analyses indicate," and I think there's two that you were referring to.

Do you happen to know, as you sit here today, what you were referring to there with meta-regression analyses, by any chance?

A. Could you tell me what page that's on?

Q. Yeah, it's 191.

A. Okay. That was my reference to meta-analysis that was performed at the meta-analysis that I reviewed.

Q. Yeah.

Do you know which one?

A. I reviewed all the ones I could find, and they're in my report.

Q. Oh, okay. So it was the prior meta-analyses in your report.

A. Yes.

Q. Got it.

Back to the questions I just asked about depression and anxiety. Are you aware that there are studies showing that the population of acetaminophen users have a much higher rate of -- the moms have a much higher

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rate of anxiety and depression?

A. I've seen studies specific to neuroticism. I'm not sure in regards to anxiety and depression.

Q. Okay. You didn't have any citation in your report to any study like that, right?

A. Initially, no. I did review some of the work -- or some of the references by Dr. Chung in that regard.

Q. Okay. Have you ever seen a study by Bandoli? Does that sound familiar to you?

A. I need to see the study to let you know.

Q. Okay. I'm going to mark it and hand it to you.

MS. JOHNSTON: 18?

MR. MURDICA: It's going to be 18, yeah.

(Cabrera Exhibit 18 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Doctor, you now have in front of you what's been marked as Exhibit 18.

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Take as long as you need to review it. I can tell you that my question is going to be on page 5 under the topic -- under the section Characteristics of Women By Duration of Use.

Do you want to go off the record, Doctor?

A. I just finished.

Q. Oh, okay.

Okay. Doctor, I know your counsel had volunteered that he had reviewed this paper before today and knew it by name and year, but I take it Dr. Cabrera didn't know about?

A. I had looked over it in regards to some of the interactions.

Q. Okay. And you see, and I directed you to the section, that the -- in this study of the 1,515 women who reported prospectively acetaminophen use during pregnancy, the ones that had the longest use were more likely, among other things, to report depression or anxiety, right?

A. That is consistent with the fourth paragraph on page 5.

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Q. Okay. And is the possibility of confounding from the symptoms of depression and anxiety in long-term users during pregnancy something you considered in your opinions before you rendered them?
A. Inasmuch as these are things that could be influencing the population. They would also -- with the expectation that a particular exposure to a -- to acetaminophen could have some correlations with depression, anxiety or mental health. I'm not aware that depression, anxiety or mental health themselves can cause the condition of ADHD or ASD in the offspring.
Q. Notwithstanding that, Dr. Cabrera, in this study, at least, long-term users were different than other users in terms of their weight, their tobacco use, their use of antidepressants in pregnancy and their depression and anxiety, right?
A. Right. So, well, weight, it should be adjusted for. And as I already mentioned, potentially alcohol or smoking should be adjusted for.

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Q. And the studies you looked at didn't adjust for depression or anxiety, correct?
A. Some of them -- I have to look specifically in that regard, but using measures of depression or anxiety, I don't recall those specifically mentioned variables in the studies I reviewed.
Q. Okay. And those are not things that Dr. Cabrera adjusted for in his causation analysis when evaluating the studies, correct?
A. As I indicated, I'm unaware that depression or anxiety in and of themselves can cause an adverse outcome in the offspring.
Q. So accordingly, you didn't adjust for it, right?
A. I didn't know that they're a risk factor in that regard. And as I mentioned, unless they're associated with a risk exposure and then those should be adjusted for.
Q. Okay. Dr. Cabrera, in your review of human autism studies, did you note

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that one of the studies that you cited, Richey from this year, determined that there wasn't enough homogeneity among the autism data that's out there in humans to conduct a meta-analysis?
A. Are you -- are you referring to the -- the heterogeneity analysis in Richey?
Q. Yes.
A. I am familiar with that Richey analysis in regard to the -- they refer to as a heterogeneity analysis.
Q. Okay.
A. Typically indicated as an I-squared value.
Q. Right.
The data wasn't similar enough to put it all together in a meta-analysis in plain language, correct?
A. There was -- there was -- and I don't know about it wasn't similar enough, but there was -- the studies have been conducted in different ways to create some difficulties in that regard.
Q. Right.
And you don't deny that Richey,

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at least, determined that it wasn't possible to do a meta-analysis on the existing human data with autism and acetaminophen?
A. I mean, we can look specifically at Richey. I don't -- I don't think I drew any specific conclusions in regards to what Richey said about that. We can look at it specifically, though.
Q. Okay. You don't recall whether or not Richey determined that a meta-analysis couldn't be done?
A. Well, they did a meta-analysis. I think you're asking me some very specifics about the meta-analysis that they did, and I think we should look at the study if you want to discuss specifics about Richey.
(Cabrera Exhibit 19 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. If I have time, we will.
I'm going to move to the next one first.
We talked about meconium earlier, and you know there's a meconium study with respect to ADHD and acetaminophen,

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right, Doctor?
A. Yes, I do.
Q. And this is -- do you see it's in front of you marked as Exhibit 19?
A. Yes, I do.
Q. And this is something that you looked at and relied on in your paper, right?
A. Yes, it is.
Q. And, in fact, this is something that you changed regarding this paper in your amended report, right, we talked about earlier.
A. I -- I did mention as far as the period of exposure, that was consistent with meconium.
Q. Okay. If you turn to page 5 of Exhibit 19, I'm going to ask you a question on the third paragraph -- a couple questions, actually.
So my first question is this, the authors of this study write, "No single observational study is sufficient for causal inference, and more observational studies using direct measurements of fetal acetaminophen exposure are needed."

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Do you see that sentence?
A. Yes, I do.
Q. Okay. Do you agree with that, as of the publication date of this article?
A. I -- at the time there was only, I believe, the one cord blood study in regard to -- actually, this is -- well, it depends on the endpoint.
So there was -- for ADHD -- well, as far as measuring concentrations, we had the cord blood study that we already mentioned.
And so we would prefer to have some sort of replication in that regards.
Q. Right.
These authors thought that more observational studies were needed using direct measurements of fetal acetaminophen exposure to reach causal inference, correct?
A. And that is what they say, yes.
Q. And that was as of 2020, correct, September 28, 2020?
A. That is what is indicated, yes.
Q. Okay. In going down a couple sentences, it says, "Third, no prior studies

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have examined the potential mechanisms mediating the association of prenatal acetaminophen exposure with neurodevelopment, a key component for assessing the potential for causation."
Did I read that correctly?
A. I -- you did, yes.
Q. Okay. And as of September 28, 2020, do you disagree with that?
A. I would say there had been numerous mechanistic studies, but nothing that had put all of the steps in regards to neurodevelopmental toxicity together.
Q. Okay. By the way, do you know any of the authors of this study?
A. I'm familiar with Andrea Baccarelli.
Q. And you know Baccarelli is one of the plaintiffs' experts in this litigation, right?
A. I'm aware.
Q. Okay. You don't disagree with Dr. Baccarelli's statements that I just read to you?
A. I do not.

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Q. Okay. Dr. Baccarelli and his colleagues include a strengths and limitations section at the end of the article.
My question for you is, on page 11 where Dr. Baccarelli and his colleagues write, "Another possibility is confounding by unknown genetic, social and familial factors associated with acetaminophen use."
Just -- sorry.
A. Where exactly?
Q. Yeah.
A. Last page?
Q. Yeah. About halfway down from the top.
A. Got it.
Q. Do you see that sentence, "Another possibility is confounding by unknown genetic, social and familial factors associated with acetaminophen use"?
A. Yes, I do.
Q. Okay. And do you acknowledge that that's a possibility?
A. I acknowledge that it's a

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possibility. I also knowledge that he followed that up with, "This concern has been recently addressed with negative control exposure analysis, maternal acetaminophen -- acetaminophen use before and after pregnancy and a partner's acetaminophen use were not associated with child ADHD in populations in which maternal acetaminophen use during pregnancy increased the risk."

Q. Right.

And my question is, Dr. Baccarelli and colleagues are acknowledging that unknown genetic, social and familial factors associated with acetaminophen use are still a possibility, although he cites one study that he believes addresses it, correct?

MS. KING: Objection to form.

THE WITNESS: To be clear, he actually cites three studies that refute that, that being both the negative control exposure studies.

And then he follows that by saying, "Furthermore, our study population has high genetic and

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sociodemographic homogeneity."

So he's rejecting that possibility also within reference 50 as well.

QUESTIONS BY MR. MURDICA:

Q. Okay. If you look at the first sentence on this page, Dr. Cabrera, Dr. Baccarelli and colleagues also write, "Confounding by unmeasured or unknown risk factors is always a possibility."

Correct?

A. He did write that.

Q. Do you disagree with him on that?

A. Well, I will make the general statement, there's always the potential for residual confounding, and I believe that's what he's referencing there.

Q. Yeah. And that's what Dr. Chung attributes the associations in some of the studies to, right?

A. Right, but it's -- based on the analysis that's been done, it's not sufficient to account for the increased risk that's been reported in multiple studies.

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Q. I -- that's what Dr. Cabrera believes, correct?

A. That's the reality we live in.

Q. Okay. Well, Dr. Cabrera, you've seen today that I've shown you everybody in the world disagrees with you except other plaintiffs' experts?

MS. KING: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. So I appreciate your answer, but I'll ask Dr. Baccarelli about this in two weeks.

MS. KING: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. Do you disagree, Dr. Cabrera, with this sentence that Dr. Baccarelli and colleagues wrote, "confounding by unmeasured our unknown factors is always a possibility in relation to the effects observed in this study"?

A. As I indicated, I -- my reading of that is that he's indicating he's -- or referencing unmeasured confounding and as a -- or unknown confounding, and so that's -- it is a possibility.

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You can't control every variable in that regard, but they've also accounted for that as well.

Q. They accounted for -- oh, really? They unaccounted for unmeasured and unknown factors?

A. Well, you can't -- you can't account for the unknown.

Q. Okay.

A. But the whole point is through using their methods of analysis, they're, I would say, mitigating that as much as possible.

Q. Okay. But they didn't write that because they don't believe it's a possibility, right?

A. You don't -- you don't know what you don't know that.

Q. Okay. We can agree on that, Dr. Cabrera.

All right. Let's go on to the next one.

All right. Dr. Cabrera, do you agree that 70 percent of adverse birth outcomes are of an unknown cause?

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MS. KING: Objection. Form.
THE WITNESS: Can you repeat the question?
QUESTIONS BY MR. MURDICA:
Q. Sure.
Dr. Cabrera, do you believe that 70 percent of adverse birth outcomes are of an unknown -- or from an unknown cause?
A. I believe I have indicated that before.
Q. You've testified to that before under oath, correct?
A. That's correct.
Q. Okay. And you stand by that?
A. I would say that over time we learn more, and over time, that percentage has gotten smaller.
Q. Do you agree that most issues with the fetal-developing brain are for as-yet unknown reasons?
MS. KING: Objection. Form.
THE WITNESS: We -- as -- over time, we've learned more about the particular genetic and environmental factors can impact those.

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And I would say it's -- it would be fair that we're maybe approaching, and we can determine risks, both environmental and genetic, for the majority of cases now.
QUESTIONS BY MR. MURDICA:
Q. Okay. Understanding that when you said it under oath five years ago, you believed it was true then, right?
A. Yes.
Q. Okay. When you said under oath five years ago that animal -- knockout animal models haven't been fruitful in converting to human effect, did you mean that?
MS. KING: Objection. Form.
If you're going to quote from his testimony, I would ask that you show it to him.
MR. MURDICA: Okay.
QUESTIONS BY MR. MURDICA:
Q. Do you agree with that or no?
A. I think our knockout models have done fairly well in some regards for animal models of human disease.
Q. Has that changed in the last

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five years?
A. Well, there -- there's still mouse models in that regard, but I think they are informative into understanding the -- particularly when we find rare mutations, and we make animal models.
I'm currently working on a mouse model with the rare gene mutation that's also associated with autism, and the animal model has been very informative.
Q. And that's changed in the last five years?
A. It's on a case-by-case basis.
(Cabrera Exhibit 20 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Last exhibit. We talked a little bit about Ystrom.
Do you remember that, Dr. Cabrera?
A. Yes.
Q. Mark that.
You should have Exhibit 20 in front of you now, Dr. Cabrera.
A. Yes, I do.

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MS. KING: Can I have a copy?
MR. MURDICA: Yes.
QUESTIONS BY MR. MURDICA:
Q. All right. Dr. Cabrera, do you remember I asked you if impulsivity was associated with acetaminophen use during pregnancy?
A. Yes, I do.
Q. Okay. If you look on page 2 in the second column, will you agree with me that this group found that that -- previously found that that was the case?
It's the second sentence in the middle column on page 2.
A. I do see that, yes.
Q. Okay. And assuming that's true -- well, they obviously claim they found it, and they have a citation, right?
A. They do.
Q. Have you looked at that citation, Doctor?
A. Yeah. I believe they're referencing their previous work.
Q. Okay. Is that a potential sign of confounding that you need to count --

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account for?
A. Impulsivity?
Q. A trait in the maternal population that uses acetaminophen that seems to be common.
A. I --
MS. KING: Objection. Form.
THE WITNESS: As I previously indicated, I -- I'm unaware that impulsivity as a trait can necessarily lead to adverse outcome.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, impulsivity could be a symptom of an underlying condition that could be associated with the two outcomes we are interested in, correct?
MS. KING: Objection. Form.
THE WITNESS: I would say that there's -- impulsivity could be -- there could be overlap between ADHD and impulsivity.
QUESTIONS BY MR. MURDICA:
Q. Okay. If you'd turn to Table 1.
This is the -- essentially the

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outcome table from their study, right?
A. Yes, it is.
Q. Okay. And if you look at the far right, the last row, last column for mothers who were exposed to acetaminophen in all three trimesters, the adjusted confidence interval is not statistically significant, correct?
A. In the fully adjusted model, it's -- there's still an increased risk. It's 1.27, and confidence interval goes from 0.99 to 1.63. It would not be statistically significant based on --
Q. And if you look --
A. -- crossing 1.
Q. Thank you, Dr. Cabrera.
And if you look further up in that column, you'll see there's quite a bit of inconsistency between uses in the different trimesters.
For example, there's no statistical significance for use in the second and third or first and third trimester, but there is for the first and second trimesters.

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Right?
MS. KING: Objection. Form.
THE WITNESS: I will say there is consistency in that there's an increased risk in each one of their models, in regards to model 1, model 2 and model 3, consistently show an increased risk, although not consistently statistically significant.
QUESTIONS BY MR. MURDICA:
Q. Right.
In fact, in their adjusted model, the majority of the outcomes are not statistically significant, right?
A. In their fully adjusted model, as they have applied more adjustments, the odds ratios remain positive, but there appears to be three that would not cross 1 in regards to their confidence intervals.
Q. Well, if you look at the far right, there's more than three, right? Only one -- only three of them do have statistical significance, right?
A. Right. That's three of them do

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not cross 1.
Q. Okay. Sorry.
The rest of them, Dr. Cabrera, so seven or eight of them, are not statistically significant, right?
A. Still an increase in risk, but they're not statistically significant.
Q. Okay. And this is another one of those studies where all this document is used at some particular time for some particular duration in a trimester, not a length of use or the actual portion of the trimester when the use was, correct?
A. Yes. So this -- their analysis is largely based on duration of use. It doesn't necessarily tell you within a trimester when it was used.
Q. And that's unfortunate from a perspective of a teratologist like yourself, right?
MS. KING: Objection. Form.
THE WITNESS: The more information we have on the dose and the duration and the frequency of exposure, the better.

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QUESTIONS BY MR. MURDICA:
Q. Okay. And if we turn to the very end of the study in conclusions, the last two sentences -- the last sentence the authors conclude, "We do not provide definitive evidence for or against a causal relation between maternal use of acetaminophen and ADHD."
Do you see that?
A. I do see that.
Q. And based on the table we just saw, you would agree, would you not, Dr. Cabrera, that this study in and of itself doesn't provide evidence for or against a causal relationship between acetaminophen and ADHD, correct?
A. An individual study typically isn't going to provide enough data to demonstrate a causal relation in that regard.
MR. MURDICA: Okay.
Anything else?
All right. I don't have anything else.
Do you have any questions, Rebecca?

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Oh, Sean's going to do it.
MR. WATTS: Sean, wake up.
MR. TRACEY: Yeah, I think I'm going to do it. Can we take, like, a five-minute break?
THE WITNESS: Please.
MR. TRACEY: Or do you want to just roll now?
MR. WATTS: No, he wants to take a five-minute break and go to the restroom.
MS. KING: Five minutes? Is it really five minutes?
VIDEOGRAPHER: Off the record, 5:36.
(Off the record at 5:36 p.m.)
VIDEOGRAPHER: The time is 5:49 p.m., back on the record. Beginning of Media 8.
CROSS-EXAMINATION
QUESTIONS BY MR. TRACEY:
Q. Hi, Dr. Cabrera. How are you?
A. I'm doing well.
Q. I've got a few -- my name is Sean Tracey, as you know. You and I have

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known each other for years, haven't we?
A. Yes, we have.
Q. I've got a few questions that I want to ask you, and the first one is, you have a lab called that's the Finnell/Cabrera lab; is that right?
A. The Finnell/Cabrera Birth Defects Research Laboratory.
Q. And what academic -- is that associated with any academic institutions?
A. That's at Baylor College of Medicine.
Q. Okay. And prior to Baylor College of Medicine, was it affiliated with another academic institution?
A. Prior to that, we were at the University of Texas at Austin --
Q. And --
A. -- and also part of the Dell Medical School.
Q. And are you known as a principal investigator?
A. Yes, I am.
Q. What's a principal investigator?

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A. That means I lead National Institutes of Health-funded research.
Q. And what is the National Institutes of Health?
A. Well, it's the governing body of our health sciences in the United States.
Q. And what is the primary purpose of the Finnell/Cabrera lab at Baylor College of Medicine?
A. It's our -- our catch slogan is prevention of preventable birth defects.
Q. Okay. And you mentioned your boss a few times during the deposition.
Is that Rick Finnell?
A. Yes, it is.
Q. And what is Rick Finnell's job?
A. He's a clinical geneticist by training, and currently the -- also a co-PI in the laboratory and a chair in the -- in our department.
Q. And how long have you worked with Rick Finnell professionally?
A. I met Rick Finnell in 1995 as an undergraduate student when I was appointed to his lab by his wife as part of the honors

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program at Texas A&M University.
Q. Okay. What percentage of the work at your lab deals in some form or fashion with genetics?
A. I would say the majority of the work we do has -- deals with genetics.
Q. But you're a teratologist, right?
A. That is correct.
Q. How does -- how does genetics, if it does, intersect with teratology?
A. So part of what we do is we often start by looking at particular chemical exposures, and then we look for what's called gene environment interactions. And that is particular changes in genetics that increase the risk for an adverse outcome with an exposure.
Q. And that's what you do in your lab, that's your day job.
A. That's the bread and butter.
Q. Okay. Do you remember during your -- Mr. Murdica's examination, he brought up this toxicogenomic database in the context of talking about some other databases.

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Do you remember that?
A. Yes, I do.
Q. And are we in a position where we can pull up the database and put it on the screen share?
A. I would be happy to.
Q. Because what you -- what Mr. Murdica had in front of you were printout of screenshots, right?
A. That's correct.
Q. But this is the actual live database, right?
A. Yes, it is.
Q. And if we go over to home -- oh, sorry. If you go over to CT -- yeah, go to about us. There you go.
I want you to explain to the judge and the jury what is the CTD, the comparative toxicogenomic's database?
A. So as described in the overview, that "CTD is a robust, publicly available database that aims to advance understanding about how environmental exposures affect human health. It provides manually curated information about

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chemical-gene/protein interactions, chemical-disease and gene-disease relationships. These data are integrated with functional and pathway data to aid in the development of hypotheses about the mechanisms underlying environmentally influenced diseases."
Q. Let me stop you there for a second.
That section that says "chemical-gene/protein interactions," is that what you do every day at your lab?
MR. MURDICA: Object to the form.
THE WITNESS: Yes, that's what I described just previously as gene environment interactions.
QUESTIONS BY MR. TRACEY:
Q. Okay. And then the next sentence says, "We also have additional ongoing projects involving manual curation of the exposome data and chemical-phenotype relationships to help identify pre-disease biomarkers resulting from experimental {sic} exposures."

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Do you know what that means?
A. Yes, I do.
Q. What does that mean?
A. So the exposome is the idea that similar to a lot of the other OMIC data, in the environment we're exposed to a lot of different compounds that can influence, what's referred here, as chemical and phenotype relationships. And the idea is that these models can be used to help drive research looking at potential biomarkers that may be indicative of particular exposures.
Q. Okay. And then it says, the next sentence says, "The initial release of the CTD was November 12, 2004."
And then under Support, it says, "This program is supported by funds from the National Institutes of Environmental Health Sciences."
Do you know what that is?
A. Yes, I do.
Q. What is that?
A. That's an institute under the National Institutes of Health that specifically focuses on the effects of

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environments on health.
Q. Okay. So this database is supported by the federal government.
MR. MURDICA: Objection to the form.
THE WITNESS: The NIH and the NIEHS are part of the federal government.
QUESTIONS BY MR. TRACEY:
Q. And the NIH is who you told us a few minutes ago gave you the grants.
A. They do fund my research, yes.
Q. Yeah.
And then they go on to say, "We're also proud to be part of the NIEHS Environmental Health Science Center at NC State, the Center for Human Health and the Environment."
And are you familiar with that organization at NC State?
A. I haven't been there, but apparently they have a program project there that's funding their center, similar to what we have at Baylor.
Q. Okay. And then just quickly

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scroll down, they've got data categories, because we're going to look at some of these. Mr. Murdica had the printouts, and we're going to look at the realtime search.
They say the data categories they have are chemicals, diseases, genes, phenotypes and chemical-gene/protein interactions.
Is there any more?
If we scroll down, is there more?
A. Well, the last one would be anatomy they have here for their references. It's also in the figure.
Q. Okay. And you mentioned phenotypes, and I think y'all talked about it today, but nobody defined it.
What's a phenotype?
A. So the genotype-phenotype relationship would be best characterized by Mendelian genetics where the phenotype of a plant can be shorter or tall in regards to the genes are the genotype that control whether the plant was short or tall, and short or tall is the phenotype. So that's

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just the presentation that we see is the phenotype.
Q. Okay. Now, if we scroll back up, and we want to do what you did in your report -- for example, if you go over and you -- under Search, can you click on Search?
A. Well, this is what I would do. I would put chemicals --
Q. Okay.
A. -- here, and I can type in --
Q. But I want you to start with Disease.
A. Oh, I can do diseases as well.
And I can --
Q. And type in "autism spectrum disorder," and I want you to tell us what shows up and why it's important.
A. So it defines autism spectrum disorder as a continuum of associated cognitive and neurobehavioral disorders, including, but not limited to, three core-defining features, impairments of socialization, impairments of verbal and nonverbal communication, and restricted and repetitive patterns of behavior, according to

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the DSM-5.
Q. And then it's got a bunch of tabs up there, and you can click on these and get information; is that right?
A. That is correct.
Q. And so if you click on "chemicals" -- let's do that, and tell us what shows up.
A. So the top hit is valproic acid followed by acetaminophen.
Q. Okay. And valproic acid, you and Mr. Murdica talked about, didn't you?
A. Yes, we have.
Q. You -- I thought I heard you say, that's actually the model for causing autism.
A. That is correct.
Q. And so on this Comparative Toxicogenomics Database, when you type in the disease autism, does it mean that the number one chemical interaction is valproic acid?
MR. MURDICA: Objection to form.
THE WITNESS: Based on the direct evidence of mechanistic

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interactions, valproic acid is the number one chemical.
QUESTIONS BY MR. TRACEY:
Q. And is there a general -- is it generally accepted in the medical and scientific community, or the teratology community, that valproic acid causes autism spectrum disorder?
A. Yes.
Q. Have you yourself proven that in your lab?
A. We've tested that in animal model, yes.
Q. Okay. Number two on the list is acetaminophen.
A. That's correct.
Q. And we're going to come back to that.
Number three is Bisphenol A. What is that?
A. That's a monitor -- monomer that used to be used in the production of plastics.
Q. And was that removed from plastics?

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A. It was banned.
Q. It was banned by who?
A. The federal government.
Q. Okay. Is that known and generally understood to be associated with autism spectrum disorder?
A. There were concerns that it could potentially increase risk for endocrine disruption and autism spectrum disorder.
Q. Okay. 6 and 7, I'm just going to get you to highlight because you talked about them with Mr. Murdica in terms of confounding.
And that's air pollutants in particular -- particulate matter, right?
A. That's correct.
Q. And is there some evidence that air pollutants and particulate matter may contribute to cause autism?
A. Yes, there is.
Q. Okay. Folic acid is number 9. I know you know a lot about folic acid, right?
A. Yes, I do.
Q. What is folic acid?

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A. Folic acid is a provitamin in the production of vitamin B9, which are a family of folates, which are considered essential vitamins.
Q. And does folic acid cause autism?
A. It does not. Its indication there is that use of folic acid has been shown to reduce the risk of autism.
Q. And Rick Finnell was one of the pioneers in that research, wasn't he?
MR. MURDICA: Objection to form.
THE WITNESS: So we have done some work in regards to the neural tube defect decreased risk and autism as well in regards to interaction with folate.
QUESTIONS BY MR. TRACEY:
Q. And do you know, Dr. Cabrera, whether it is recommended for all pregnant mothers in the United States to take folic acid to, in part, reduce the risk of autism?
A. Originally folic acid was used to fortify the food supply in order to reduce

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the risk of neural tube defects.
More recently, it's been shown to reduce the risk of autism as well.
Q. Okay. So some of the things on this list of the top ten, let's say, are associated with autism in a negative way in the sense that they cause it, and some are associated with it in a positive way in that they help reduce it; is that right?
MR. MURDICA: Object to form.
Sean, if you're going to keep making misrepresentations and lead like this, you just got to stop. You're testifying.
MR. TRACEY: Well, Dr. Cabrera --
MR. MURDICA: You got to stop, Sean.
QUESTIONS BY MR. TRACEY:
Q. Dr. Cabrera, tell us what it means when I see valproic acid, acetaminophen, bisphenol A, et cetera, on this -- on this chart from the toxicogenomic databases, why is this important to you in your opinion?

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A. Well, there's --
MR. MURDICA: Objection to form.
THE WITNESS: -- two parts. One in that it's showing that there's, what we refer to, as direct evidence for an interaction between valproic acid and the disease.
And that's indicated here when you highlight over this -- M is for mechanistic interactions.
And then also, it will identify genes that have been previously associated or been shown to cause or increase the risk of autism that have also been shown to be influenced by exposure to either valproic acid or acetaminophen.
QUESTIONS BY MR. TRACEY:
Q. And do you see -- can you go back to that? There you go.
So that score, valproic acid and autism has a score of 264.59, right?
A. That's correct.
Q. And there are 50 references

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there to the right, and there's 311 genes there under the Inference Network, right?
A. That is correct.
Q. And there is no question in the medical and scientific community that valproic acid causes autism, is there?
MR. MURDICA: Object to the form.
Sean, you can't testify. I mean, that's not the way this works.
QUESTIONS BY MR. TRACEY:
Q. Can you answer my question, Dr. Cabrera?
A. There was no question.
Q. Okay. Now, when you were -- when Mr. Murdica was showing you the 35 and the references and he clicked on that and he did a little -- when we look at these studies, we don't see any mention of acetaminophen or Tylenol.
Do you remember that?
A. Yes, I do.
Q. And you told him later on he wasn't doing it right.
Do you remember that?

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A. Yes.
Q. And so I want you to show the judge and the jury how to do this right so they can understand your testimony.
MR. MURDICA: Objection to form. That's not a question.
MR. TRACEY: It is.
QUESTIONS BY MR. TRACEY:
Q. Can you show us how to do this right, Dr. Cabrera, so that we can see how this database funded by the federal government shows that acetaminophen interacts with genes and is associated with autism?
A. Yes, I can.
And so as an example here, if you click on the genes that are indicated in the network, those genes come up. They're part of a gene list where if you look at a database, or actually even within this database, there are genes that have been associated with or been shown to cause autism.
And if you click on an individual gene, as an example, it will then show you the references that support those

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interactions.
And so I'll use an example here of clicking on COMT, one of the ones that we mentioned, or clicking on capicua, CIC, where they ask where it was in the database. If you click on that, it then opens up the reference that indicates "acetaminophen affects the expression of capicua messenger RNA," and it provides you with a reference.
And if you click on that reference, it will then provide you the study that shows that acetaminophen was used in hepatotoxicity, as I indicated in my report, and shows the change in expression for capicua.
And that can be done with any of the genes in that -- in the gene family. So it could also be done with COMT as I'd also mentioned, and you'll get changes in COMT as well. And you can do that with any of the genes in the list.
That's where the references are.
Q. Is it true, Doctor, and we can do some more if we need to, but if I -- you

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click on any one of those genes --
And that's what those are, genes, right?
A. That's correct.
Q. -- there is studies in this federally supported database that link the exposure to acetaminophen to either the downregulation or the upregulation of the expression of these genes?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. TRACEY:
Q. Is that right?
A. There are studies for each one of those genes. They'll be supported -- there will be studies that support that acetaminophen changes their expression. And you can also filter that if you want to look particularly at upregulation, or increase in expression, or downregulation, or decrease expression.
Q. Okay. And the score there for acetaminophen and autism is 231, and the score for valproic acid is 264.
A. That is correct.

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MR. MURDICA: Objection --
QUESTIONS BY MR. TRACEY:
Q. Is that right?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. TRACEY:
Q. The inference score.
Is that right?
A. That is correct.
Q. And in terms -- what is an "inference score"?
A. So --
MR. MURDICA: Objection to form.
THE WITNESS: So as indicated, that's querying the database. It shows you the strength of this interaction.
QUESTIONS BY MR. TRACEY:
Q. And so number 1, the highest inference score is valproic acid. Number 2 is acetaminophen.
MR. MURDICA: There's no question. Objection to form.

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QUESTIONS BY MR. TRACEY:
Q. Is that right?
A. That is correct.
Q. It is a question.
A. And there's two parts of this.
So partially sorted by direct evidence and then by the inference score, those are highest reported interactions.
Q. Okay. Let's do something. Does anybody in the world that you know of think that ibuprofen causes autism?
A. Not that I'm aware.
Q. Let's do something just for fun. Let's go back and type in "ibuprofen" and see if autism comes up.
A. You want to look at diseases?
Q. Diseases, yeah.
Do you see any autism there?
A. I do not see that as a -- at least as a top hit, and the inferences scores are rather low.
Q. And then if you go to hypertension, that's number one for ibuprofen?
A. That is correct.

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Q. Do you know whether or not ibuprofen is associated with hypertension?
A. It is associated with hypertension. It's one of the reasons why it's contraindicated in late pregnancy.
Q. Okay. Okay.
Now, how did you use this database, if you did, to support your opinion?
A. I used it to -- actually, and largely in response to criticism that was brought up by Dr. Chung in regards to having no gene or gene-drug interactions identified in the literature.
Q. Okay. And this is the proof that that's false.
MR. MURDICA: Objection to form.
THE WITNESS: So --
QUESTIONS BY MR. TRACEY:
Q. Is that right?
A. As indicated in my report, this data does report that there are overlapping etiology in regards to genes between ADHD and ASD, and I reported that in my report.

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Q. Can you go back to the main page again, just for a second, then we're going to leave this.

Do you know -- do you know if Johnson & Johnson has anything to do with this database?

A. I --

MR. MURDICA: Objection.

THE WITNESS: Not that I'm aware.

QUESTIONS BY MR. TRACEY:

Q. Okay. Do you know if Johnson & Johnson gives any money to support this database?

A. Not that I'm aware.

Q. All right. Anything else we need to talk about on this database for now?

A. I think we've covered the deficiencies that I've noticed earlier.

Q. Okay. I want to flip and talk about this adverse outcome pathway for a second.

If somebody could bring up adverse outcome pathway 20 so we can put it on the screen like we did this database.

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By the way, you did -- you told Mr. Murdica what you did was a weight of the evidence analysis, correct?

A. That is correct.

Q. And weight of the evidence analysis means -- does it -- does it mean you weighed all the different lines of evidence?

A. That is correct.

Q. And is there any one piece in your weight of the evidence analysis that if it, you know, wasn't there, your opinion would crumble to dust?

MR. MURDICA: Objection to form.

THE WITNESS: Any one piece. If there were deficiencies at multiple steps, then you would be -- you would have trouble drawing conclusions.

QUESTIONS BY MR. TRACEY:

Q. Well, let me ask it this way.

If the toxicogenomic database didn't exist, would you still have the same opinion?

A. I could still draw -- I could still make the opinions in the absence of the

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database.

Q. Okay. And if the adverse outcome pathway that's been published as number 20 didn't exist, would you still have the same opinions?

A. Yes, and I would still go through the same analysis, even in the absence of adverse outcome pathway number 20.

Q. What I want to do just for fun is, can you search this pathway for the word "autism"?

A. Yes, I can.

Q. Hold on. Before you do that, before you hit -- oh, sorry. I was going to read the actual title of the pathway.

It's called "The binding of electrophilic chemicals to the SH thiol group of proteins and/or to selenoproteins involved in protection against oxidative stress during brain development leading to impairment of learning and memory."

Did I read that right?

A. That's correct.

Q. And then over to the right are a bunch of authors, right?

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A. That is correct.

Q. Do you know if any of them work for Johnson & Johnson?

A. I do not know that any of them work for Johnson & Johnson.

Q. Okay. Go back and search for "autism." I want to see whether it comes up in this document.

A. So it indicates there's 15 mentions of autism within the document.

Q. Okay. Can we -- let's just look at a couple. I don't know if you can make that bigger. I'm blind, and I have some my glasses on.

A. That good?

Q. So there's a reference that says, "The relationship between mercury and autism, a comprehensive review and discussion." And that's referenced in this paper?

A. That is correct.

Q. And then down below, it's got "Landa, diagnosis of autism spectrum disorders in the first three years of life."

That's another one?

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A. Yes.
Q. Let's go to the next one. "The role of epigenetic change in autism spectrum disorders," and that's in the Frontiers of Neurology, there at the top page 23? "The role of epigenetic change in autism spectrum" -- oh.
A. I -- yes.
Q. It's a stream site, isn't it? Yeah.
A. Yes, it is.
Q. Okay. Do you know whether or not epigenetic change has been associated with autism?
MR. MURDICA: Objection to form.
THE WITNESS: Yes, I do know it has been associated.
QUESTIONS BY MR. TRACEY:
Q. Okay. In your lab, do you spend a great deal of your time studying and researching epigenetic changes?
MR. MURDICA: Objection to form.
THE WITNESS: Yes, we do. We

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recently published an epigenetic study looking at the interaction of folate or folic acid specifically on epigenetic changes in the animal model or mice.
QUESTIONS BY MR. TRACEY:
Q. Okay. Keep clicking. Let's see what else comes up in this adverse outcome pathway on autism.
Okay. "The putative role of environmental mercury and the pathogenesis and pathophysiology of autism spectrum disorders and subtypes."
What's next? There we go.
Is this in the body of the AOP here?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. TRACEY:
Q. Can we tell?
A. This is page 47 of the AOP.
Q. And they mention there in the middle, "Indeed, disruption of glutamate, signalling is thought to be part of the etiology underlying some neurodevelopmental

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disorders such as autism and schizophrenia."
Do you agree with that?
A. I -- yes, that has been reported.
Q. Okay. Same -- next paragraph, they mention autism again saying, "Genes involved in gluta -- glutamatergic pathways affecting receptor signalling metabolism and transport were enriched in genetic variants associated with autism spectrum disorder."
Is that right?
A. Yes, it is.
Q. What does that mean?
A. Simply that if you looked at those genes that have been associated with autism spectrum disorder, and that is, genes that have been known to modify or increase risk for autism, that they also overlap functionally and mechanistically with glutaminergic pathways.
Q. Just click on another one. Just go to one more through there.
There we got another paper. That may be the same guy.
A. Yeah. I think this is the

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reference that they were referencing in those studies.
Q. Yeah. Okay. Click one more in that.
"Autism and intellectual disability: Two sides of the same coin." That's referenced in this paper, isn't it?
A. Yes, it is.
Q. Now, the name of this adverse outcome pathway though isn't autism; they're talking about memory and learning, right?
A. That is correct.
Q. Do you know why autism is referenced so many times in this adverse outcome pathway that's been published and publicly available?
MR. MURDICA: Object. Object to the form.
THE WITNESS: Because there's overlap in the outcome with particular exposures and their impact on neurodevelopment that can lead to both intellectual disability, autism and other neurodevelopmental disorders, including ADHD.

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QUESTIONS BY MR. TRACEY:
Q. And do you use adverse outcome pathways in your -- in your -- during your -- in your day job?
A. I find them helpful, and the answer is yes. I find them helpful for identifying where there's deficiencies in research so that we can develop hypotheses and obtain funding to test those hypotheses.
Q. And do you teach that to students?
A. I do teach it to my students, yes.
Q. Okay. The toxicogenomic database that we were on a few minutes ago supported by the federal government, do you use that database in your day job?
A. Occasionally. When I have to look up data on a -- on a chemical that I'm researching, I'll often start with the database searches as it's normal to start with what's known in the databases, both the chemistry databases and the genetics and genomics databases.
Q. Do you remember when

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Mr. Murdica was clicking on 35 and bringing up those papers and said none of them said acetaminophen?
Do you remember that?
A. Yes, I do.
Q. How come he couldn't find acetaminophen?
A. Well, that study that's -- we were -- that I would reference in regard to Santos was a methodology. It's describing the method I was using.
It wasn't describing the genetic analysis that I did, which you have to click on the genes in order to look at the genetic analysis.
Q. So he was just in the wrong place?
A. That is correct.
Q. Okay. Do you -- Dr. Cabrera, you're familiar with the peer review process?
A. Yes, I am.
Q. What is the peer review process?
A. If you want to publish a paper that is going to be in a reputable,

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scientific journal, then it's -- it will be sent out by multiple reviewers, and that's part of what we refer to as the peer review process.
We find reviewers for a paper based on common publications of those reviewers with the topic of the publication, and then they review it and criticize it or find deficiencies in it.
And that gets returned back to the author to correct or to respond to those criticisms in order to have the paper meet an expected scientific standard.
Q. Okay. And have you yourself been a peer reviewer?
A. I've acted as both peer reviewer and editor for various journals.
Q. And on the topic of birth defects or adverse birth outcomes?
A. Yes. I've been guest editor for Birth Defects Research, and I'm currently acting as a guest editor for Reproductive Toxicology.
Q. And so you -- you've done what -- you've been the peer reviewer where

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you looked at somebody else's scientific work; you made edits; you made comments; you asked questions, right?
A. I still do that as well, yes.
Q. And you yourself -- you've had your homework graded when you've submitted it to peer review by other experts in the field, haven't you?
A. Yes, I have.
Q. And all that is part of the scientific process that is so important to worldwide scientific knowledge, isn't it?
MR. MURDICA: Objection to form.
You're doing it again, Sean. See if you can ask a non-leading question. You're obligated to.
MR. TRACEY: Okay. I'm trying to move us out of here quickly, but, Robert --
MR. MURDICA: Doesn't -- doesn't feel that way.
QUESTIONS BY MR. TRACEY:
Q. Tell us why the peer review process is important.

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A. It's important that the research meets a standard and that people that are proficient in the field can understand it and potentially reproduce it.

In order for -- to provide that information, it needs to be reviewed by others to meet that standard.

Q. Okay. And you participate and support the peer review process; is that right?

A. Yes, I do.

Q. Mr. Murdica showed you a document, I think it might be Exhibit 17, but was that a peer review of AOP 20?

A. Yes, that has been peer-reviewed as well.

Q. Okay. Anything in that peer review that you read on your break that alters one word of your opinion?

MR. MURDICA: Objection to form.

THE WITNESS: No, there's not.

QUESTIONS BY MR. TRACEY:

Q. Okay. That looked like a typical peer review process?

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A. Well, they -- some of them can be pretty intense, so I would say it was -- it was a -- maybe an average -- yeah, an average peer review process.

Q. Okay. All right. All of your opinions that you've given and gave in your report are based on reasonable scientific certainty?

A. Yes. All the opinions I've given have been provided within a reasonable degree of scientific certainty.

Q. Tell me what percentage of your adult life you've been engaged in trying to find out the cause of and ways to prevent birth defects.

A. Actually, all of my adult life I've been working either in genetics or birth defects research.

Q. Your entire professional life?

A. Yeah, starting as an undergraduate and continuing on thereafter.

MR. TRACEY: And -- okay. All right. Dr. Cabrera, I'll save the rest for later. Thank you.

I'll pass the witness.

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REDIRECT EXAMINATION

QUESTIONS BY MR. MURDICA:

Q. Dr. Cabrera, do you stand by the answers that you gave me under oath so far today?

A. I do.

Q. Okay. Mr. Tracey started asking you questions, several of them, about Rick Finnell and Rick Finnell's qualifications and lab you share with Rick Finnell.

Do you remember those?

A. Yes.

Q. You also know, Dr. Cabrera, that Rick Finnell has taken a lot of money from Sean Tracey and other plaintiffs' lawyers involved in this litigation, right?

MS. KING: Objection, form.

MR. TRACEY: Object to the form.

THE WITNESS: I don't -- I don't know how much money he's received.

QUESTIONS BY MR. MURDICA:

Q. You know that Mr. Tracey has

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hired him for other birth defect litigation, right?

MR. TRACEY: Object to the form.

THE WITNESS: I -- I'm aware.

QUESTIONS BY MR. MURDICA:

Q. You're aware. You've testified under oath about it before, right?

A. I'm aware.

Q. Okay. And it goes, you got into this business of taking money from plaintiffs' lawyers from Dr. Finnell who originally was the one taking money from plaintiffs' lawyers, right?

MS. KING: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. He got you into it?

A. To be clear, Richard Finnell has worked with both the defense and plaintiffs in the past and has been -- because I recall he's been retained in the past also by defense.

Particularly I think he was actually on a panel for Johnson & Johnson in the past.

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Q. You testified under oath before that he did one case for one defendant for a short amount of time.

Do you remember testifying to that in 2018?

A. As I just indicated.

Q. Okay. And you know that Dr. Finnell has worked for plaintiffs' lawyers on birth defect cases. By and large that's been his expert involvement in litigation, right?

A. He has done that, yes.

Q. And that's how you got introduced to this, right?

A. We used to have a company together.

Q. Okay. When you brought up the database onto the computer screen, one of the things Mr. Tracey had you read was the base -- the background on the database, and it said -- well, you read into the record that it was intended to aid with the development of hypotheses.

Correct?

A. That's correct.

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Q. And that's what you used it for, right?

A. Initially, as I just told you, I looked at that database in order to see if there -- if and how many genes there were that were common to the etiology of ADHD and ASD.

Q. Right.

And what the database says -- there's a disclaimer that I'm sure you've seen that says, this should not be used to diagnose any condition or disease, right?

A. That is correct. It's not for diagnosis.

Q. Right.

And the fact that there's a number of genes allegedly connected to a particular compound and an outcome doesn't mean that it's causative, correct?

A. That in and of itself is not enough evidence to conclude causality.

Q. And the example he showed you, you clicked on CIC. That was the first gene you clicked on, right?

A. As indicated earlier, I -- the

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question had come up about where was CIC in the database, and so that was what I clicked on to show you.

Q. And it gave the Beyer article, which we previously marked as an exhibit, right?

A. That's correct.

Q. And you weren't able to show where CIC was in the article, correct?

A. I told you it was in the data.

Q. Right.

And we didn't see that on what you just brought up on the -- on the computer screen, correct?

A. We didn't -- we didn't dig that deep into the data.

Q. That didn't fill in the gap of what we were missing, right?

MS. KING: Objection. Form.

THE WITNESS: We didn't dig that deep into the data.

QUESTIONS BY MR. MURDICA:

Q. Okay. If I leave a blank in the transcript right here, will you fill in when you -- when you get -- review and sign

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the transcript, will you fill in where that mention is actually found in Beyer?

A. I can --

MS. KING: Objection. Form.

THE WITNESS: I can -- I can look into it.

QUESTIONS BY MR. MURDICA:

Q. Thank you, Doctor.

If, when we get the transcript, the blank that we're going to put is not filled in, can we agree that it doesn't exist, and it's not actually in that citation?

MS. KING: Objection. Form.

THE WITNESS: We could agree that I didn't find it.

QUESTIONS BY MR. MURDICA:

Q. Okay. Fair enough.

Mr. Tracey had you reading from -- oh, by the way, if you were to click on more of those genes, we would end up with the other article marked that was responsible for 217 of those 273, right, the one I showed you earlier?

A. Potentially.

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Q. Right.
And that -- we never found -- in two of the articles I showed you, we never found mention of the genes of the two that we actually looked at, right?
A. In that particular article, we did not see them.
Q. Right.
And that's responsible for the majority of the alleged gene interactions that Mr. Tracey had you click on, right?
A. I can certainly look into that.
Q. Okay. And if we were to open others, I'm not going to make you do it right now, but you tell me if you know this, I just clicked on, on my own computer, FMO1, which was one of those genes, and it lists a couple different references. And one says that acetaminophen upregulates FM01 and then right there, there is another reference that says acetaminophen downregulates FMO1.
You've seen that, right?
A. There are examples where the expression can change, depending on both which tissues they're testing, which cell

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lines they're testing or the dosages they're testing. You find differences in response.
Q. Yeah. There's -- you agreed with me earlier that the criteria for including a gene in that is just that some article somewhere mentions it somehow as associated in some way, right? There's a -- you could look at the listing of what words they pick up on to determine whether to include it, right?
A. It is a text-based query, and you can then sort through that text base. So if you want to look at just the genes that are downregulated, you can find that, or just the genes that are upregulated. You can also look at protein interactions if you want to look at mechanistic interactions as well.
Q. It's someone's attempt to put all the data they can find together in one place and let the viewer decide what to do with it for hypothesis generation, correct?
A. Well, it's also the state of the art right now for mining existing scientific literature for information that can be helpful for regulatory purposes.

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Q. Right.
And for identifying potential gene compound outcome interactions, right?
A. It's used that -- for that as well.
Q. Yeah.
It doesn't prove causation in any given circumstance by itself, correct?
A. By itself, currently, it does not --
Q. Okay.
A. -- demonstrate causation.
Q. Then Mr. Tracey showed you AOP 20, and he had you read the instances where the word "autism" appeared.
Do you remember that?
A. Yes, I do.
Q. Okay. And one of them he had you read about, that autism shares pathways with glute -- shares -- has commonality with glutamatergic pathways.
Do you remember that?
A. Yes, I do.
Q. Okay. And that has nothing do with this case. That's GABA, right?

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A. That is GABA.
Q. Yeah. And GABA is not one of the mechanisms of action you've postulated in any way to do with acetaminophen and the two outcomes here, right?
A. I did not discuss GABA.
Q. And when you looked carefully at what we're calling the peer review part of AOP 20, you saw clearly that the reviewers said, "Unless the authors want to change the ad" -- "the adverse outcome to autism, then they should delete it. The authors must delete the sentence in the overall assessment domain of applicability section where they refer to autism. This is not an AOP for autism, and if that's the intention, it must be changed."
You saw that when you were reviewing it, right?
MS. KING: Objection. Form.
THE WITNESS: I read that.
QUESTIONS BY MR. MURDICA:
Q. Yeah. You don't agree with Mr. Tracey that this is about autism in any way, shape or form, correct?

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MS. KING: Objection. Form.
THE WITNESS: So to be clear, the AOP still has language in regard to interaction with autism and reference with autism as an endpoint.
QUESTIONS BY MR. MURDICA:
Q. It has -- it has the mentions like what you looked at with Mr. Tracey, right?
A. In addition to what I've referenced in my report.
Q. Right.
What it -- what it doesn't say is that autism is an outcome as part of that AOP. And it's very clear, is it not, from the review, that that was not permitted to be part of it?
MS. KING: Objection. Form.
THE WITNESS: But -- I don't know about permission, but they ask that it's either -- the AOP itself be changed to autism-specific AOP, or that it be removed, and they chose to remove it.

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QUESTIONS BY MR. MURDICA:
Q. Right.
And the author acknowledged, in what we read before, that they couldn't change it to autism because there wasn't enough data to support it, correct?
MS. KING: Objection. Form.
THE WITNESS: That was, in part, what we read earlier.
MR. MURDICA: Okay. I don't have any other questions.
RECROSS-EXAMINATION
QUESTIONS BY MR. TRACEY:
Q. Dr. Cabrera, Mr. Murdica likes to talk a lot about money and plaintiffs' lawyers.
Have you noticed that?
A. I've heard it a few times.
Q. Yeah. I want to talk about money and Johnson & Johnson for a minute.
Okay?
A. Okay.
Q. Do you know whether or not Baylor College of Medicine receives money from Johnson & Johnson?

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A. Yes, they do.
Q. Do you know whether or not Baylor College of Medicine, because they receive money from Johnson & Johnson, forbid Rick Finnell from testifying in this case?
A. That is correct.
Q. What do you think of that?
MR. MURDICA: Objection to form.
THE WITNESS: Well, it's a little bit upsetting. A little bit disturbing.
QUESTIONS BY MR. TRACEY:
Q. That someone can throw their money around and stop scientists from testifying?
MR. MURDICA: Hang on. Objection to form.
THE WITNESS: That's correct.
MR. MURDICA: Sean, you said that Baylor -- you're testifying, Sean, but you're testifying that Baylor is preventing Finnell, correct?
MR. TRACEY: That's right. Because they receive money from

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Johnson & Johnson, they are preventing him from testifying in this case.
MR. MURDICA: Yeah. Okay. You don't -- you don't know that. That is improper. That is definitely not --
MR. TRACEY: I do know it, because I've seen the letter.
MR. MURDICA: Well, you're not under oath, and you're not giving witness testimony, so you need to stop.
MR. TRACEY: Well, I know. That's why I'm asking Robert Cabrera --
MR. MURDICA: You told him.
MR. TRACEY: -- because he knows it, and I need to get the testimony from him.
MR. MURDICA: I think you forgot how to ask a question, Mr. Tracey. But you need to stop.
MR. TRACEY: I've forgot -- I've forgotten so much, Jim, I don't know where to begin.

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QUESTIONS BY MR. TRACEY:
Q. But let me ask you this.
Dr. Cabrera, you know, sir, don't you, that Baylor College of Medicine refused to allow Rick Finnell to testify in this case because they receive money from Johnson & Johnson?
MR. MURDICA: Objection to the form. I mean, that is literally --
MR. TRACEY: Do you --
MR. MURDICA: Can you ask a non-leading question?
QUESTIONS BY MR. TRACEY:
Q. Let me flip it around.
Do you know whether or not Baylor College of Medicine forbid Rick Finnell from testifying in this case because they received money from Johnson & Johnson?
MR. MURDICA: Objection to form.
THE WITNESS: That is correct.
QUESTIONS BY MR. TRACEY:
Q. Okay.
A. That was the reason they gave him that he could not testify.

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Q. That was the reason they gave him.
MR. MURDICA: Objection to form.
MR. TRACEY: Sorry, I spoke over you.
QUESTIONS BY MR. TRACEY:
Q. I just want to make sure.
Is that what you said?
A. That is the reason they gave him; that he was -- that he would not be allowed to testify.
MR. MURDICA: Objection to form.
QUESTIONS BY MR. TRACEY:
Q. Okay. Do you know whether he agrees with you?
MR. MURDICA: Objection to form. This is not -- if you want Dr. Finnell, get Dr. Finnell. This is not about Dr. Finnell.
THE WITNESS: He does agree with me.
MR. TRACEY: All right. Thank you, Dr. Cabrera. Pass the witness.

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FURTHER REDIRECT EXAMINATION
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, you testified earlier that Baylor doesn't even know the crazy opinions you're espousing here, right? You never told them?
MS. KING: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Do they know you're out here creating a health hazard?
MS. KING: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, does Baylor know what you're doing?
MS. KING: Objection. Form.
MR. TRACEY: Don't answer those questions. Those are abusive and insulting and unbecoming.
QUESTIONS BY MR. MURDICA:
Q. Dr. Cabrera, does Baylor know what you're doing today and the opinions that you're offering?
A. As I already indicated, I'm on vacation today.
Q. Right.

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Did you ask Baylor anything about Dr. Finnell and whether or not he could testify in this litigation?
A. I didn't ask Baylor about what -- whether Dr. Finnell could, but he did disclose that information to me. And he told me that Baylor said that he would not be allowed to testify.
Q. So Dr. Finnell told you something that he allegedly heard from Baylor, correct?
MS. KING: Object to form.
THE WITNESS: It's not that he allegedly heard. He had communication in that regard.
QUESTIONS BY MR. MURDICA:
Q. But you did not. You didn't hear it, did you? Did you see a communication?
A. I have -- I have not seen a communication.
Q. Okay. Did Dr. Finnell ask Baylor before deciding whether or not he could do that here?
A. He asked before he could

testify.
Q. He asked, but you didn't, right?
A. I -- my conflict of interest is through my company. He was going to testify as an individual employee of Baylor.
Q. So if he had a company, it would be different?
A. As it used to be when we were part of the same company, we consulted under our company.
Q. Okay. So you were just asked questions about something that you heard third-hand from Dr. Finnell that he allegedly asked Baylor about but you didn't, right?
MS. KING: Objection. Form.
THE WITNESS: I heard firsthand from Dr. Finnell in that regard.
QUESTIONS BY MR. MURDICA:
Q. Right.
About something he allegedly heard from Baylor itself, right?
A. About his communication with Baylor.
Q. Okay.

A. He told me that it wasn't that I went out and asked him. He told me that -- about what was going on.
Q. So other people at Baylor, if they don't have a company, have to ask Baylor if they can testify as an expert, but you don't, right?
A. Anybody that has a company and files conflict of interests through their company, I have it on my disclaimer and I'm under a conflict of interest that I have to disclose what I'm doing in my company, and I have to identify whether it's creating a conflict of interest with my funded research. And if it does, then I'll have to disclose that, and that's one of the reasons why I mentioned earlier that I would not be able to do acetaminophen work at Baylor College of Medicine.
Q. And Baylor hasn't stopped you in any way from testifying here or offering your opinions, correct?
A. They have not.
MR. MURDICA: Okay. I have no further questions.

MR. TRACEY: Thanks, Dr. Cabrera.
THE WITNESS: Thank you.
VIDEOGRAPHER: Okay. Off the record. 6:38.
(Deposition concluded at 6:38 p.m.)
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CERTIFICATE

I, CARRIE A. CAMPBELL, Registered Diplomate Reporter, Certified Realtime Reporter and Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, Robert Cabrera, Ph.D. was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

_____
CARRIE A. CAMPBELL,
NCRA Registered Diplomate Reporter
Certified Realtime Reporter
California Certified Shorthand Reporter #13921
Missouri Certified Court Reporter #859
Illinois Certified Shorthand Reporter #084-004229
Texas Certified Shorthand Reporter #9328
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Louisiana Certified Court Reporter #2021012
Notary Public
Dated: August 3, 2023

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Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

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ACKNOWLEDGMENT OF DEPONENT

I, ________________________, do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____
Robert Cabrera, Ph.D. DATE

Subscribed and sworn to before me this
________ day of ________________, 20 ______.
My commission expires: ________________

Notary Public

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ERRATA

PAGE LINE CHANGE

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LAWYER'S NOTES

PAGE LINE